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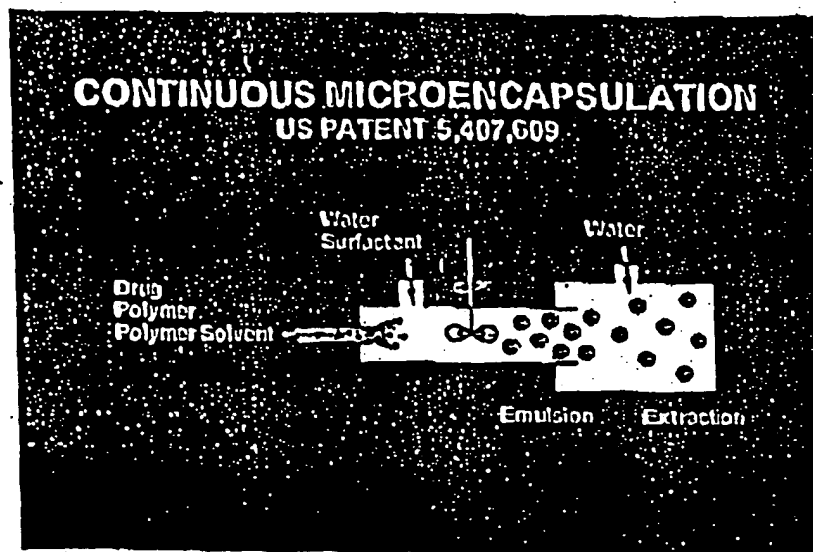
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# SOUTHERN RESEARCH'S PATENTED MICROENCAPSULATION PROCESS



## Advantages

- US Patent issued 1995
- Fast encapsulation time -- milliseconds
- Minimal exposure to polymer solvent
- High encapsulation efficiency
- Good Yields
- Makes small microparticles  
    <100 micron <10 micron

## Drugs Microencapsulated

- Proteins
- Peptides
- Small molecules
- Water-soluble drugs
- Hydrophobic drugs
- Drugs encapsulated in  
    lactide/glycolide polymers

FIGURE 1

FIGURE 2.

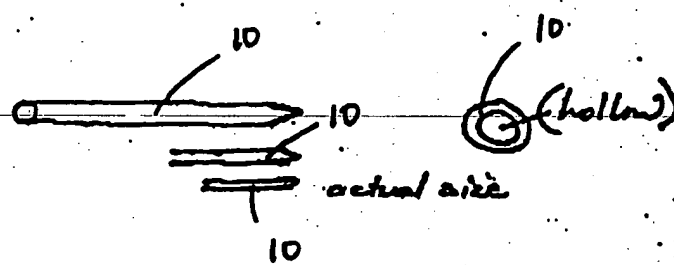
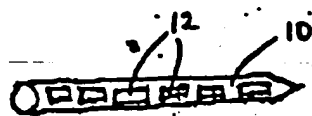
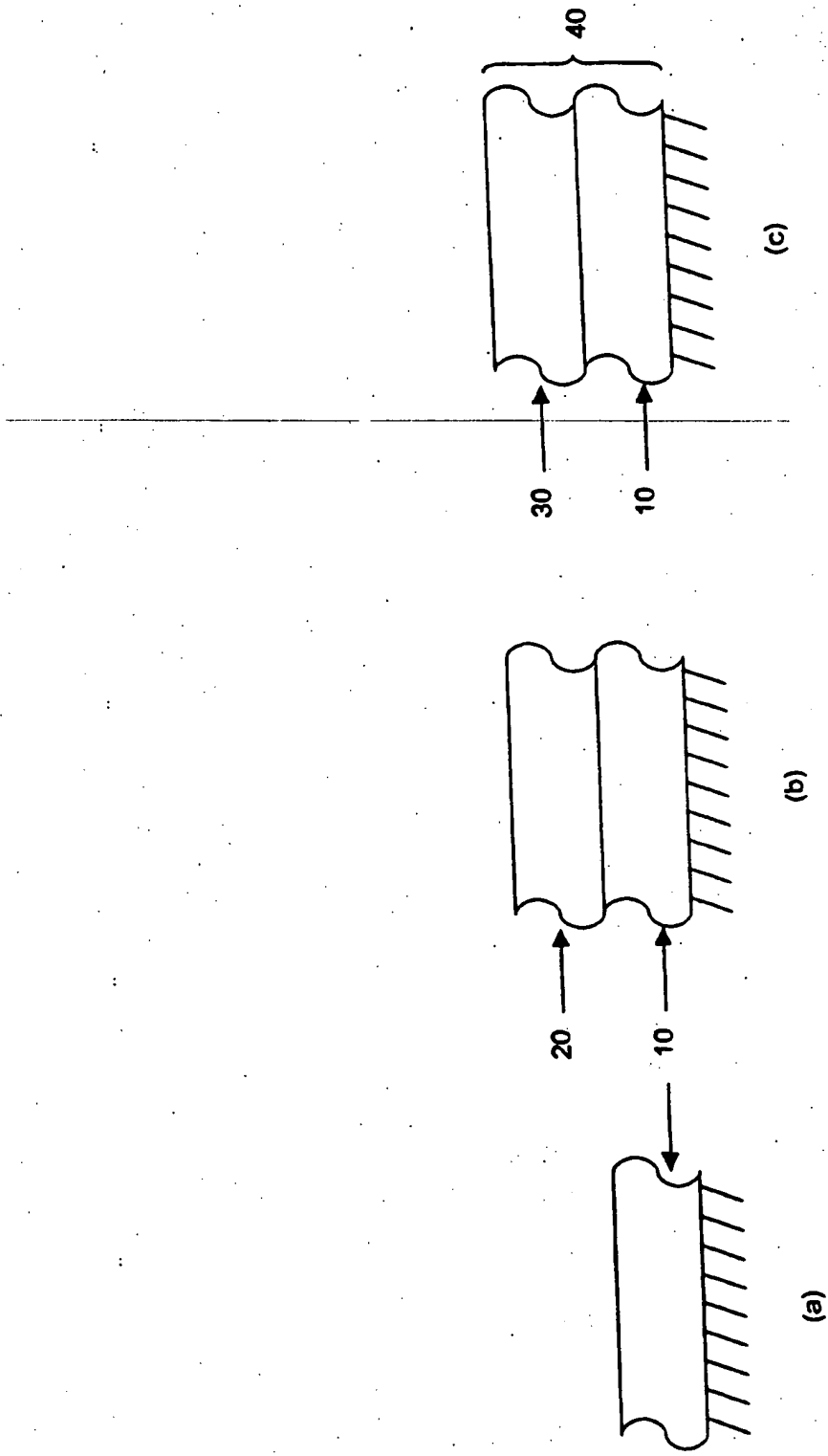


FIGURE 3





**FIGURE 4**

Conditions: Ambient

|           |       |       |       |       |                        |
|-----------|-------|-------|-------|-------|------------------------|
| Material: | PX510 | PX261 | PX749 | PX125 | PX510 + 14% Paclitaxel |
| Hardness: | F     | B     | 3B    | 4B    | F                      |

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

|           |       |       |       |       |                        |
|-----------|-------|-------|-------|-------|------------------------|
| Material: | PX510 | PX261 | PX749 | PX125 | PX510 + 14% Paclitaxel |
| Hardness: | F     | B     | 9B    | <9B   | F                      |

Hardness Rating: 2H-H-F-HB-B-2B-3B-4B-5B-6B-7B-8B-9B  
 Harder ← → Softer

FIGURE 5

Conditions: Ambient

|                        |        |        |       |       |                        |
|------------------------|--------|--------|-------|-------|------------------------|
| Material:              | PX510  | PX261  | PX749 | PX125 | PX510 + 14% Paclitaxel |
| Resistance To Cracking | < 3 mm | < 3 mm | < 3mm | < 3mm | < 3mm                  |

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

|                        |        |        |       |       |                        |
|------------------------|--------|--------|-------|-------|------------------------|
| Material:              | PX510  | PX261  | PX749 | PX125 | PX510 + 14% Paclitaxel |
| Resistance To Cracking | < 3 mm | < 3 mm | < 3mm | < 3mm | < 3mm                  |

FIGURE 6

Conditions: Ambient

|           |       |       |       |       |                        |
|-----------|-------|-------|-------|-------|------------------------|
| Material: | PX510 | PX261 | PX749 | PX125 | PX510 + 14% Paclitaxel |
| Class:    | 5B    | 5B    | 5B    | 4B    | 5B                     |

Class Rating: 5B = 0% of coating removed from substrate  
4B = Less than 5% of coating removed from substrate

**FIGURE 7**

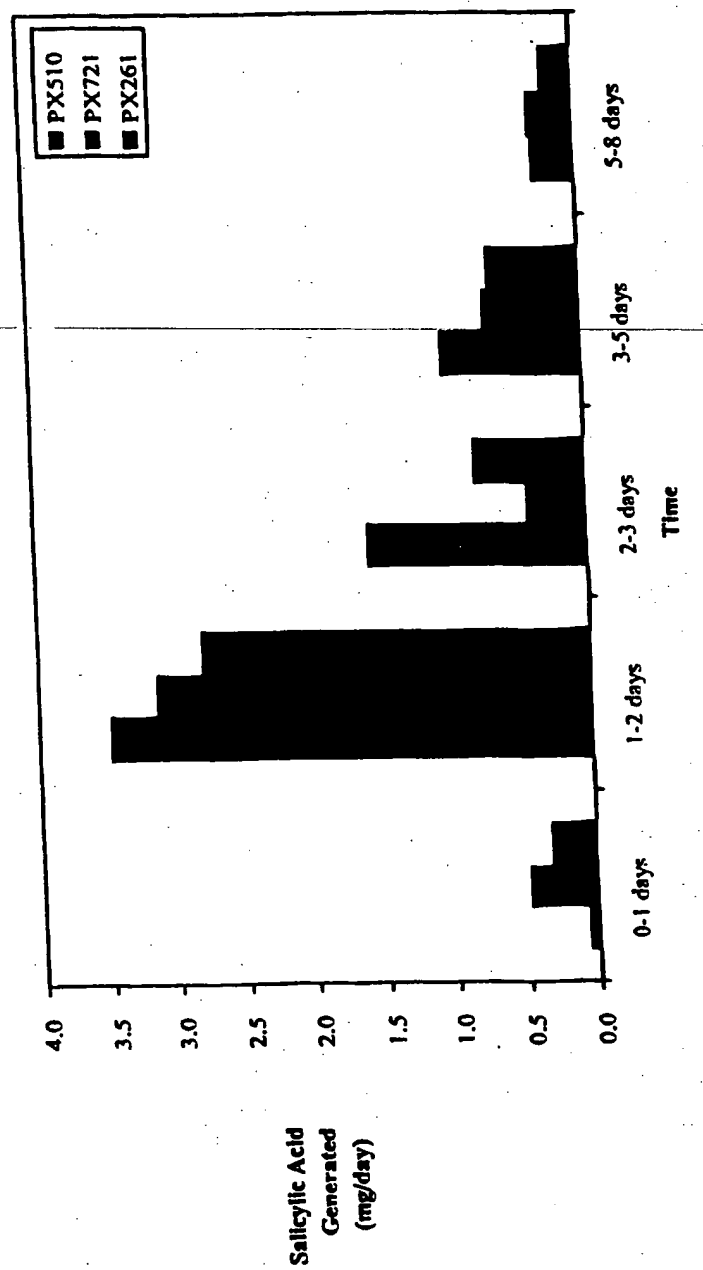


FIGURE 8A



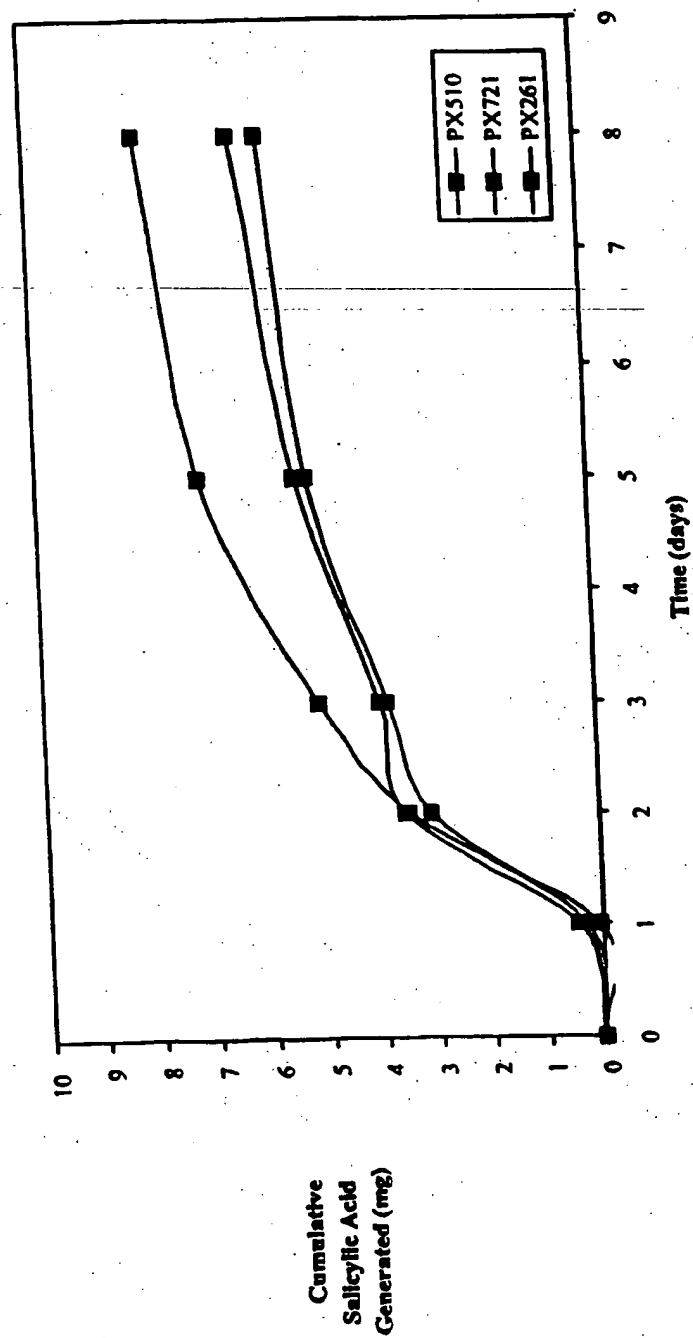


FIGURE 8B

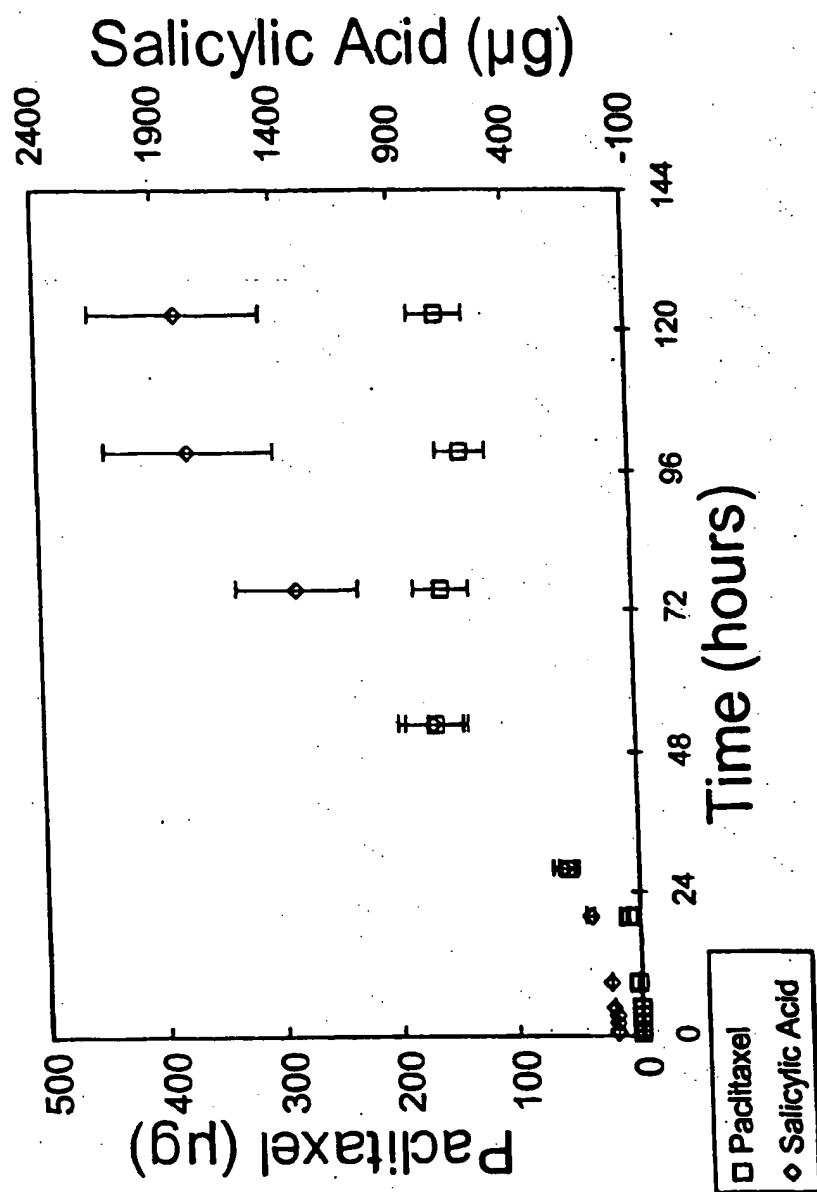


FIGURE 9A

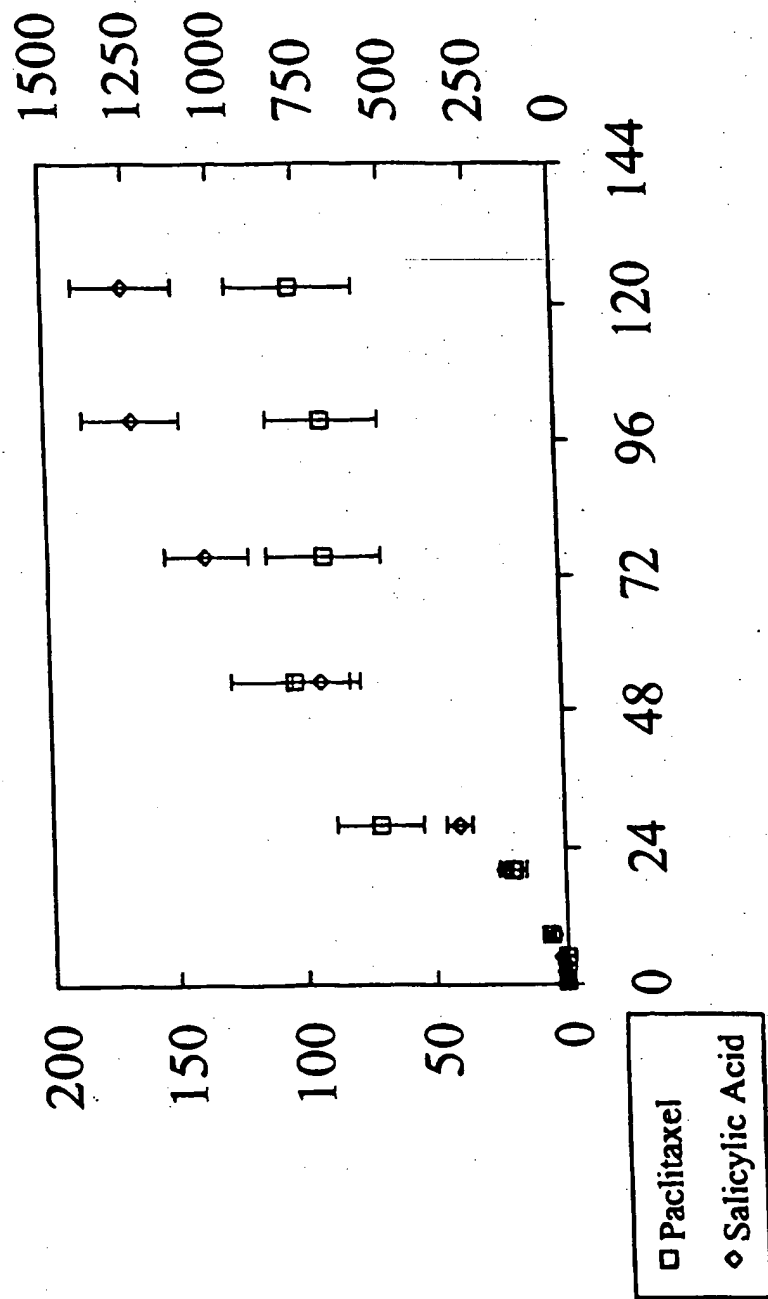
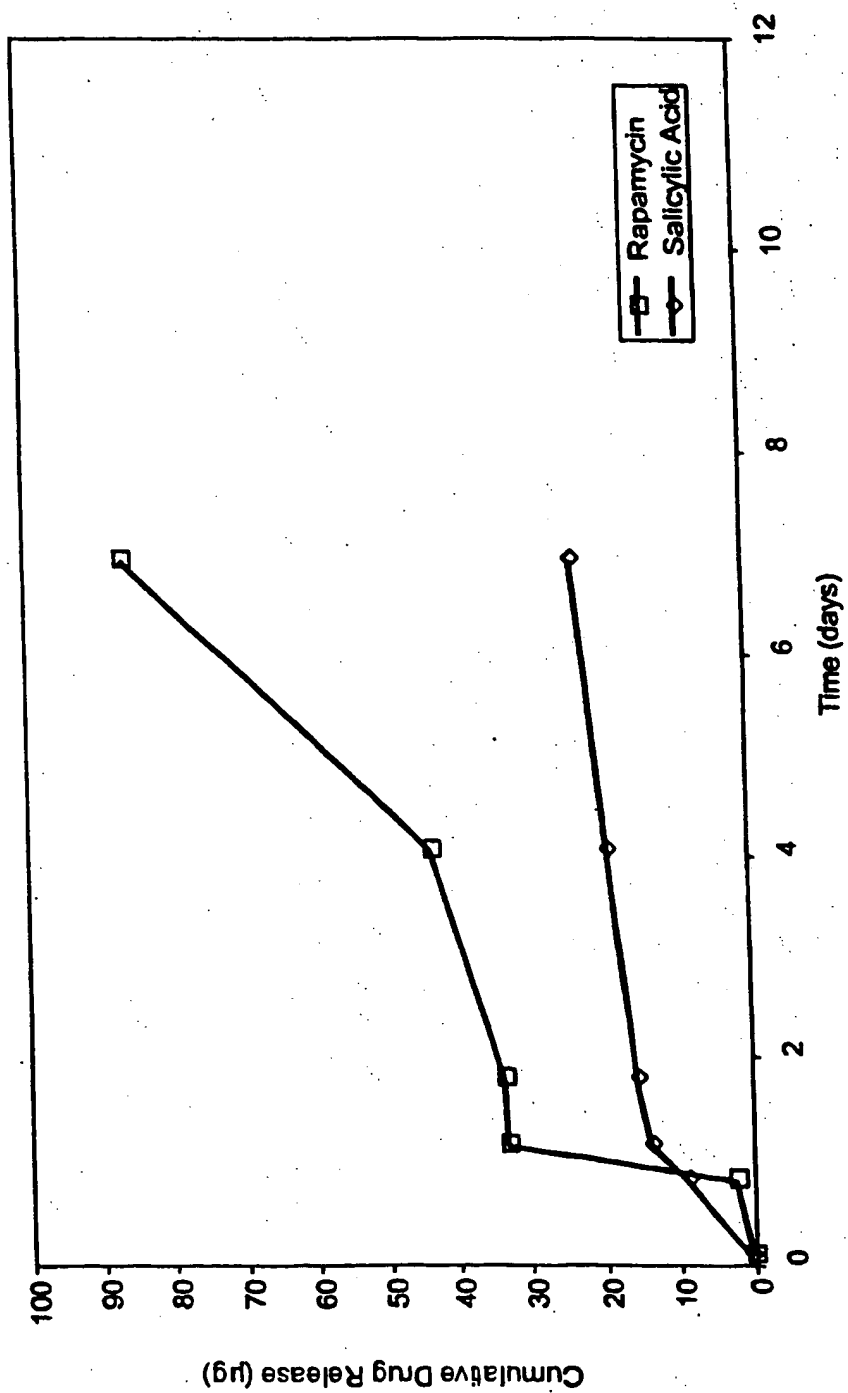


FIGURE 9B

## Formulation

| Property                | PX510                    | PX721 | PX261 | PX749      |
|-------------------------|--------------------------|-------|-------|------------|
| $T_g$ ( C )             | 44                       | 38    | 29    | 16         |
| Tensile modulus (MPa)   | 2.0 (25 C)<br>5.1 (37 C) |       |       | 3.0 (25 C) |
| Yield Strength (MPa)    | Not<br>observed          |       |       | 6.0 (25 C) |
| Ultimate Elongation (%) | 1.5 (25 C)<br>350 (37 C) |       |       | 500 (25 C) |

**FIGURE 10**

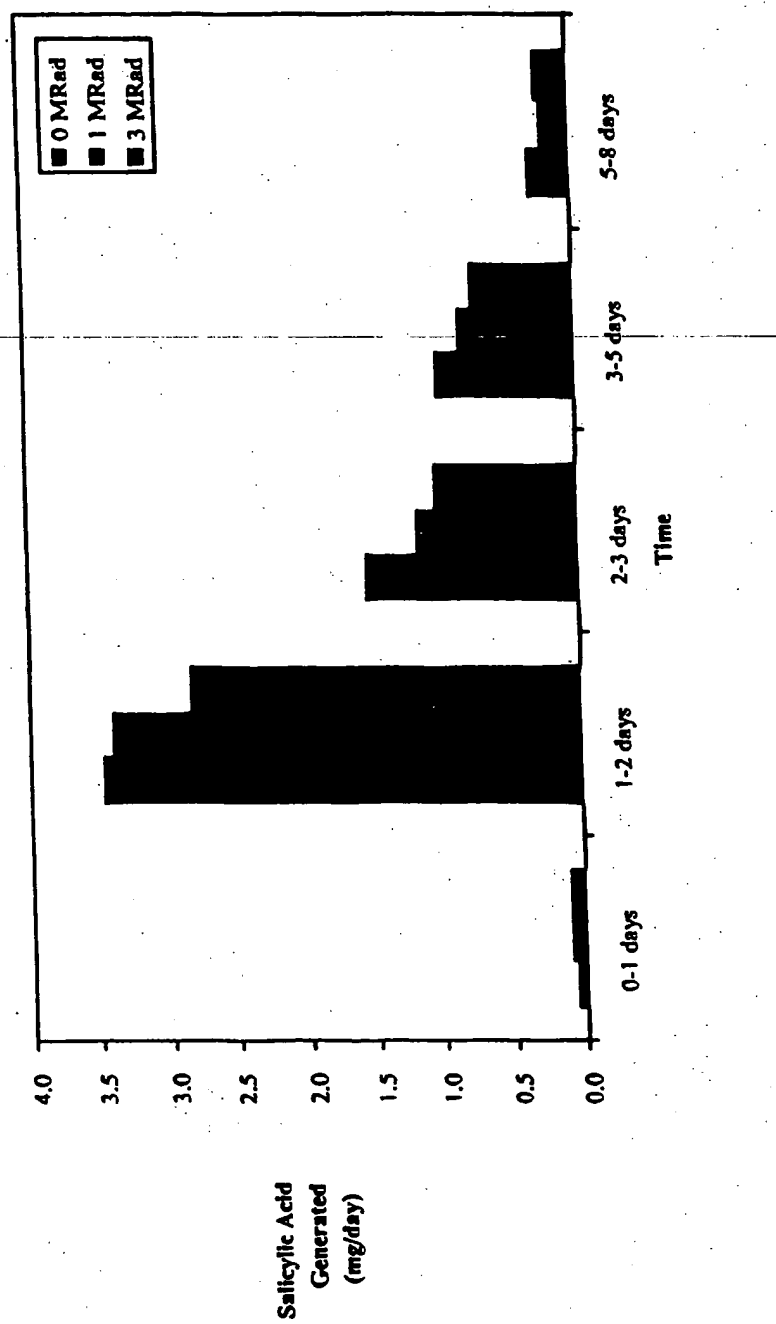


**FIGURE 11**

| E Beam (3 MRad) |          |       |         | $\gamma$ (25-35 KGys) |          |          |  |
|-----------------|----------|-------|---------|-----------------------|----------|----------|--|
| Property        | PX510    | PX721 | PX261   | PX510                 | PX721    | PX261    |  |
| MW              | -28%     | -39%  | -26%    | -14%                  | N/C      | N/C      |  |
| Hardness        | -2 units | N/C   | -1 unit | N/C                   | -3 units | -2 units |  |
| Flexibility     | N/C      | N/C   | N/C     | N/C                   | N/C      | N/C      |  |
| Adhesion        | N/C      | N/C   | -1 unit | N/C                   | N/C      | N/C      |  |

N/C: no change

**FIGURE 12**



**FIGURE 13A**

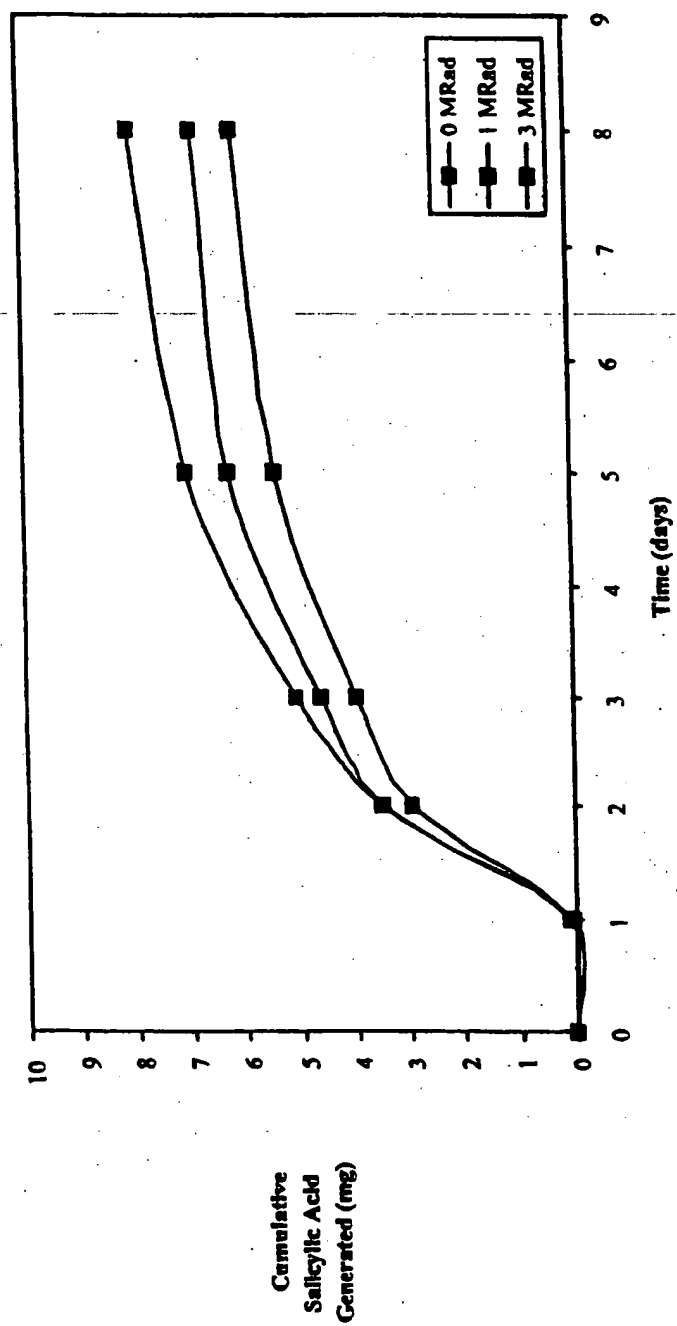


FIGURE 13B



# PX242 20-53 Coated Coupon Diflunisal Elution

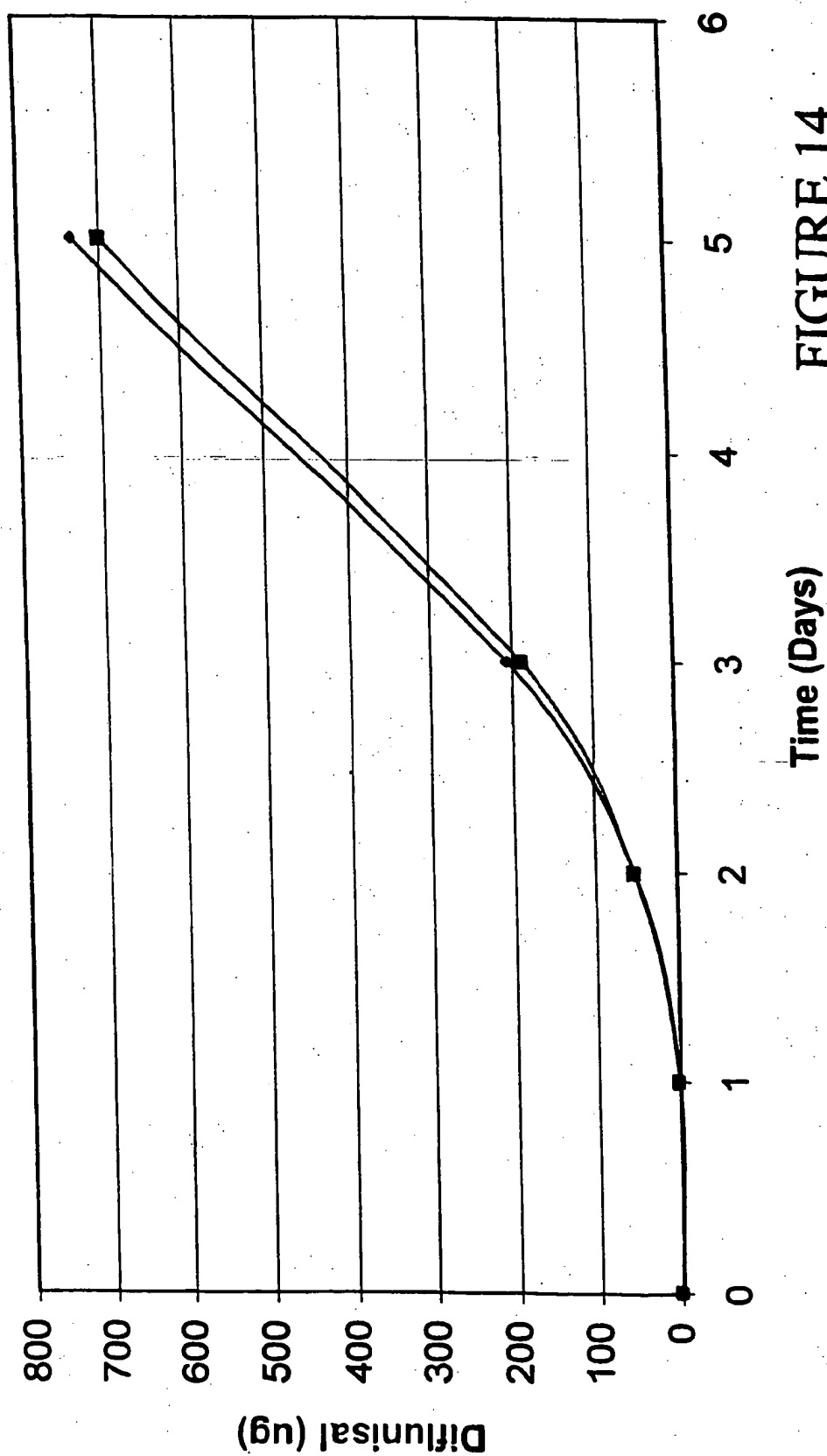


FIGURE 14

# PX242 20-53 Coated Coupon Diflunisal Elution

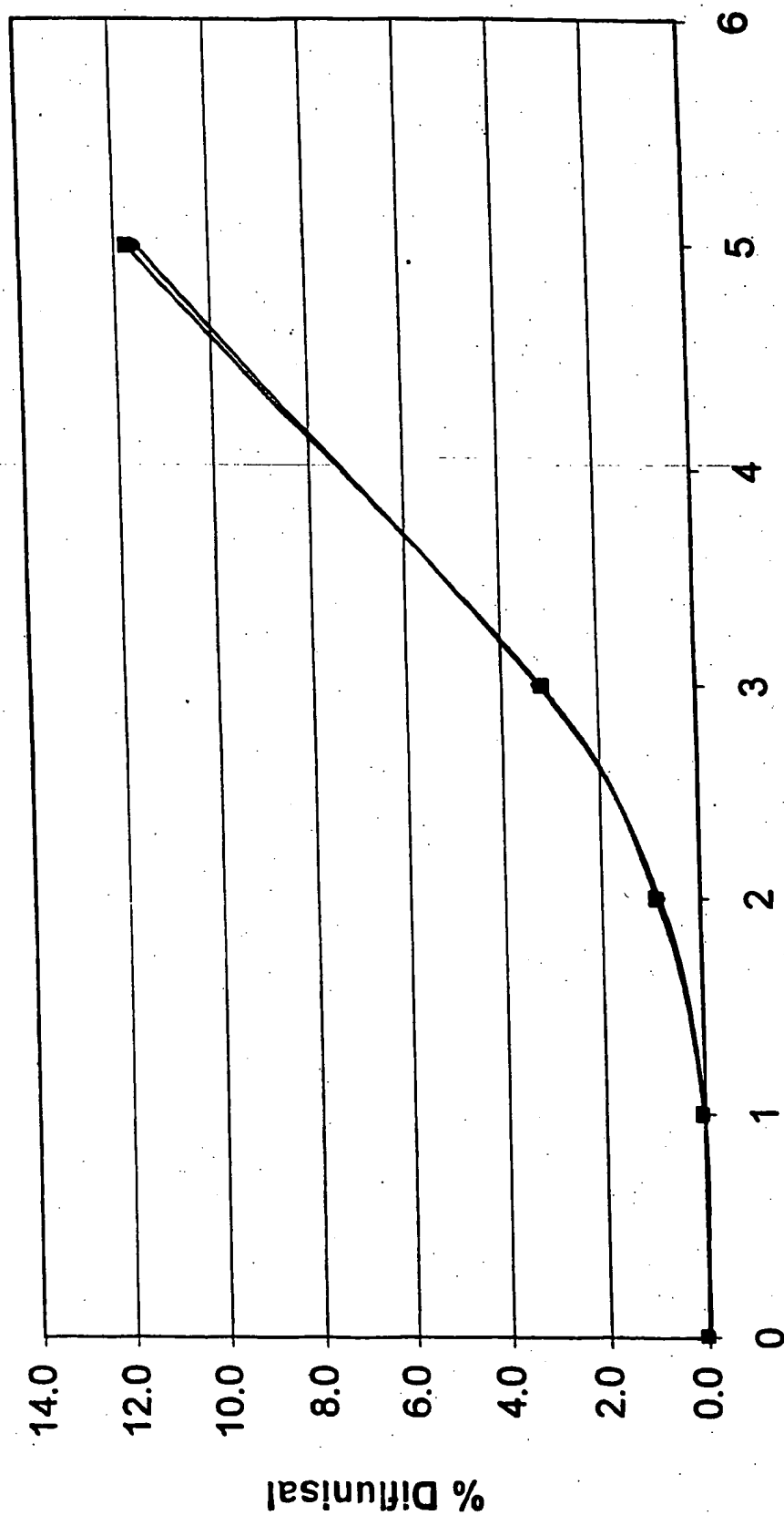
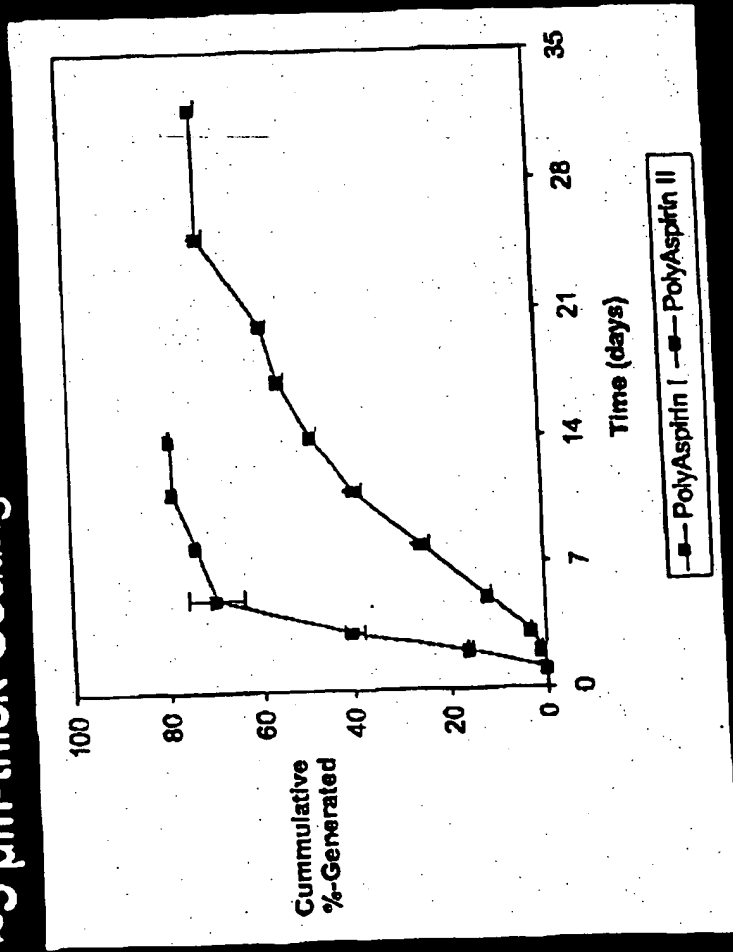


FIGURE 15

# Erosion of PolyAspirin I & II

Generation of NSAID into 37 °C pH 7.4 PBS from  
~5 µm-thick Coatings on 316L SS Plates

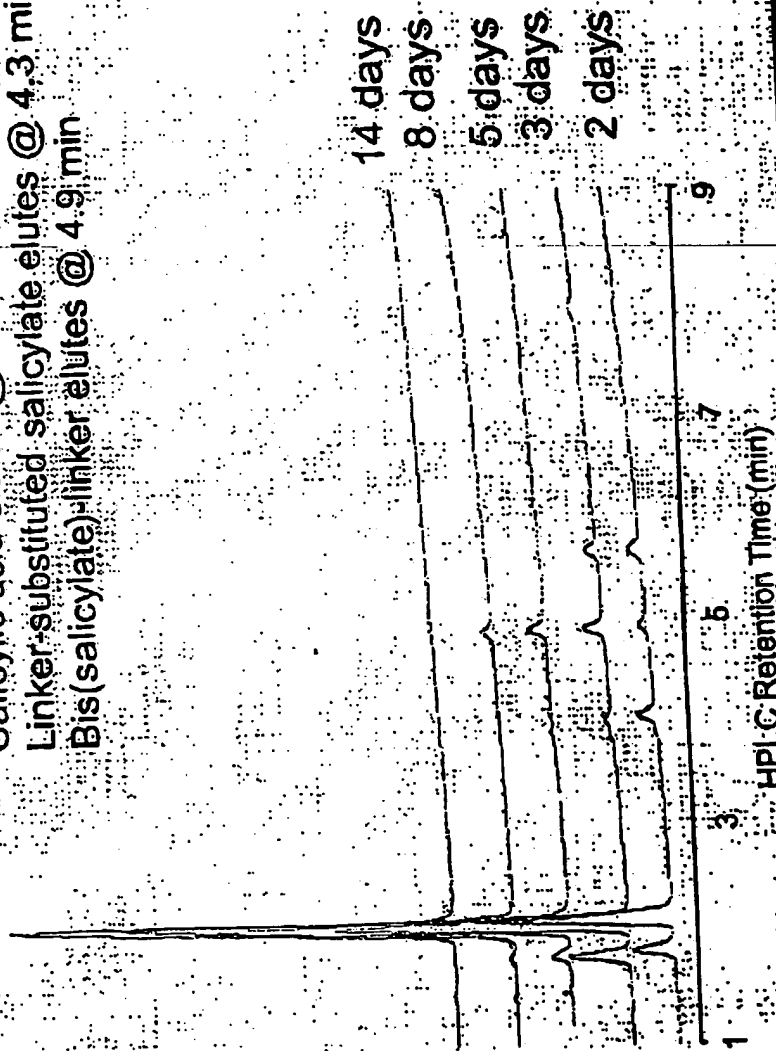


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FIG. 16

# Erosion Profile for PolyAspirin I

Salicylic acid elutes @ 2.1 min  
Linker-substituted salicylate elutes @ 4.3 min  
Bis(salicylate)-linker elutes @ 4.9 min

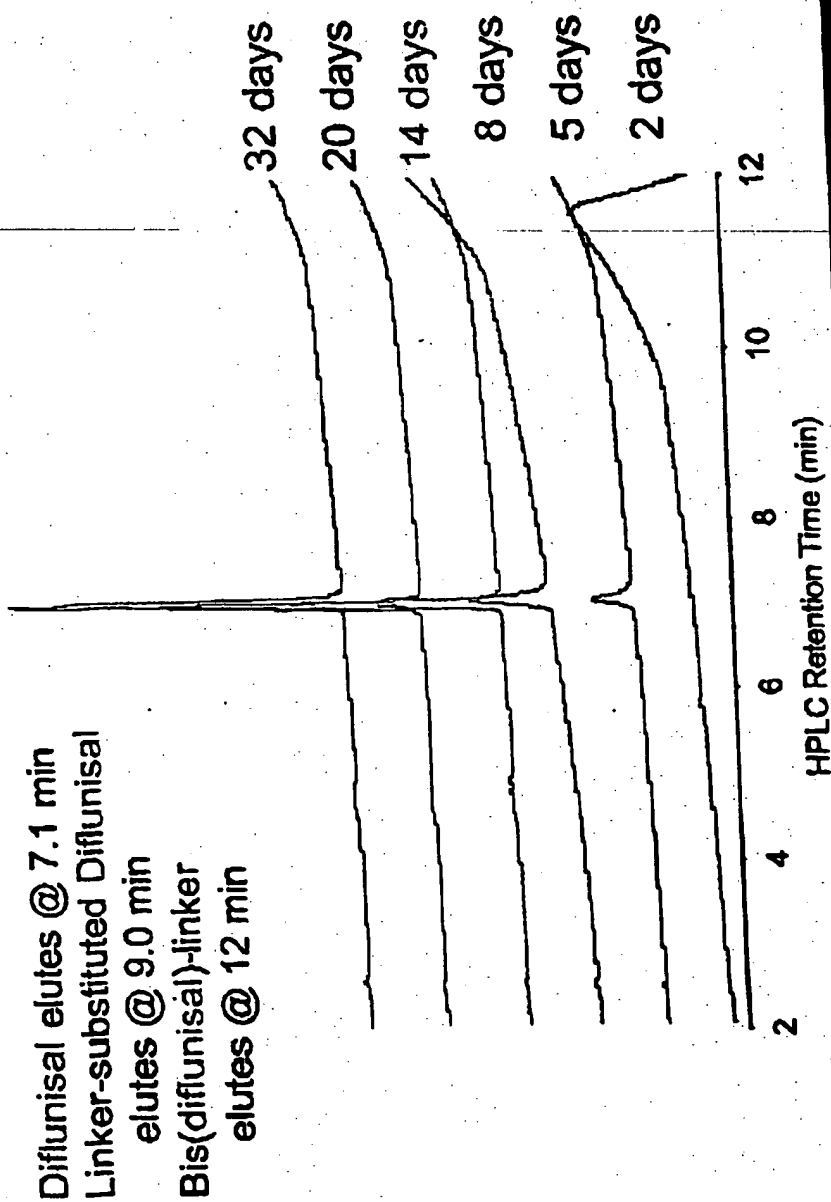


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FIG. 17

# Erosion Profile for PolyAspirin II



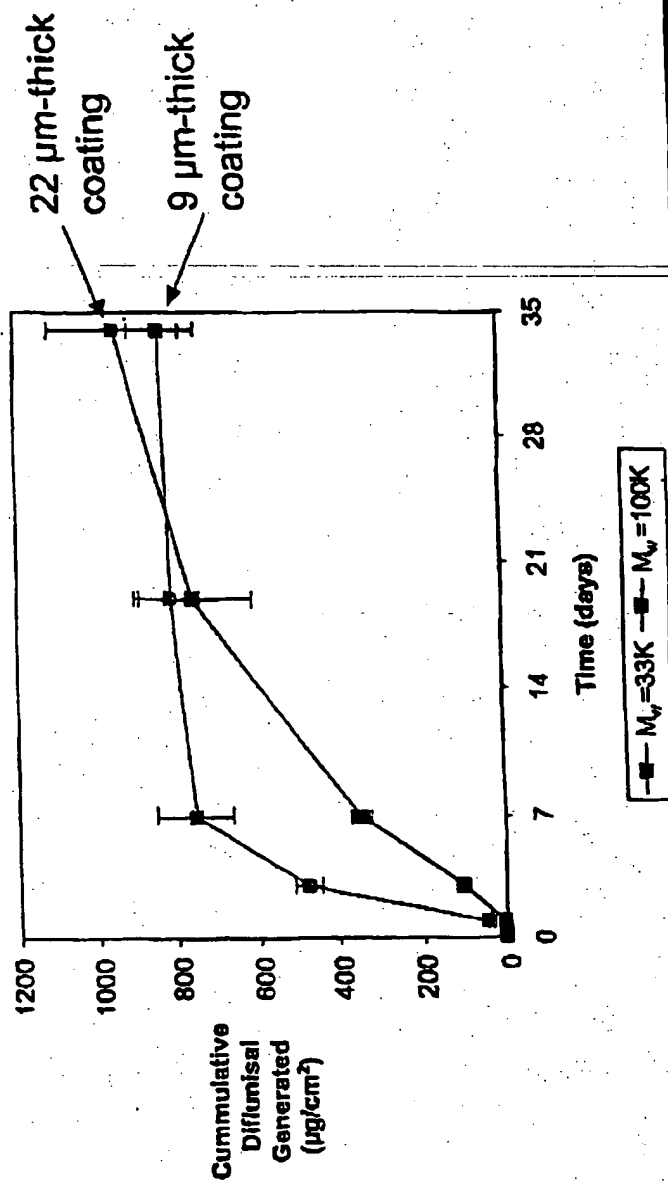
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FIG. 18

# Effect of MW on Erosion

Generation of Diflunisal from PolyAspirin II into  
37 °C Serum from Coatings on 316L SS Plates

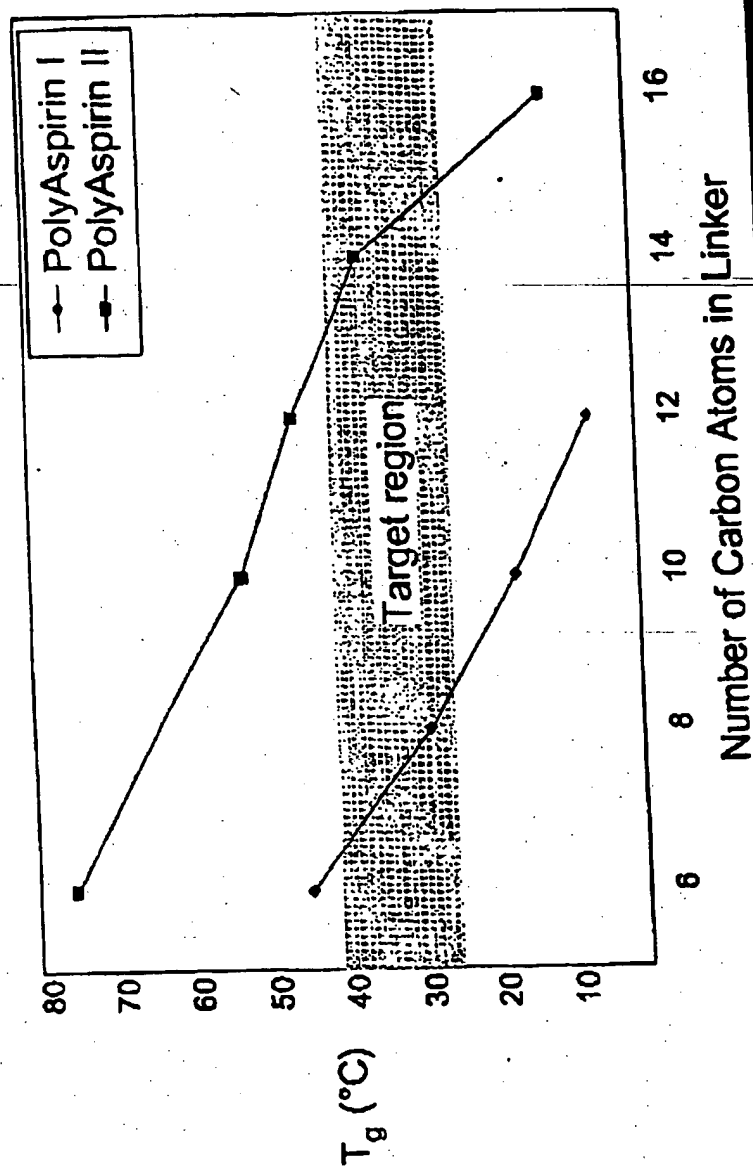


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FIG. 19

# Tuning Mechanical Properties



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FIG. 20

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# Thermoanalysis of PolyAspirin™

## PolyAspirin I      PolyAspirin II

|          |                |                 |
|----------|----------------|-----------------|
| Property | PX261          | PX657           |
|          | $M_w \sim 20K$ | $M_w \sim 100K$ |

|                         |                              |              |              |
|-------------------------|------------------------------|--------------|--------------|
|                         | 29                           | 36           | 44           |
| $T_g$ (°C)              |                              |              |              |
| Ultimate Stress (kPa)   | 1700 (25°C)<br>>2000 (37°C)  | >2800 (25°C) | >2600 (25°C) |
| Ultimate Elongation (%) | >500 (25°C)<br>>500 (37°C)   | >4 (25°C)    | >500 (25°C)  |
| Toughness (kPa)         | >3900 (25°C)<br>>4400 (37°C) | >560 (25°C)  | >4000 (25°C) |


  
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FIG. 21



# Properties of PolyAspirin™ Coatings

## PolyAspirin I      PolyAspirin II

|                |                 |
|----------------|-----------------|
| PX261          | PX657           |
| $M_w \sim 20K$ | $M_w \sim 33K$  |
|                | $M_n \sim 100K$ |

### Test

#### Hardness

Ambient

5 min in PBS, 37 °C

1 hr in PBS, 37 °C

3H  
B  
4B

F  
2B  
8B

#### Flexibility

Ambient

5 min in PBS, 37 °C

1 hr in PBS, 37 °C

<3 mm  
<3 mm  
<3 mm

<3 mm  
<3 mm  
<3 mm

#### Adhesion

Ambient

5B

5B

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PolyAspirin  
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FIG. 22

# PolyAspirin Coatings with Admixtures

PolyAspirin II (PX657)  
 No Admixture      20% Pacitaxel Admixed

## Test

### Hardness

Ambient

5 min in PBS, 37 °C  
 1 hr in PBS, 37 °C

F  
 2B  
 8B

F  
 F  
 6B

### Flexibility

Ambient

5 min in PBS, 37 °C  
 1 hr in PBS, 37 °C

<3 mm  
 <3 mm  
 <3 mm

<3 mm  
 <3 mm  
 <3 mm

### Adhesion

Ambient

5B

5B

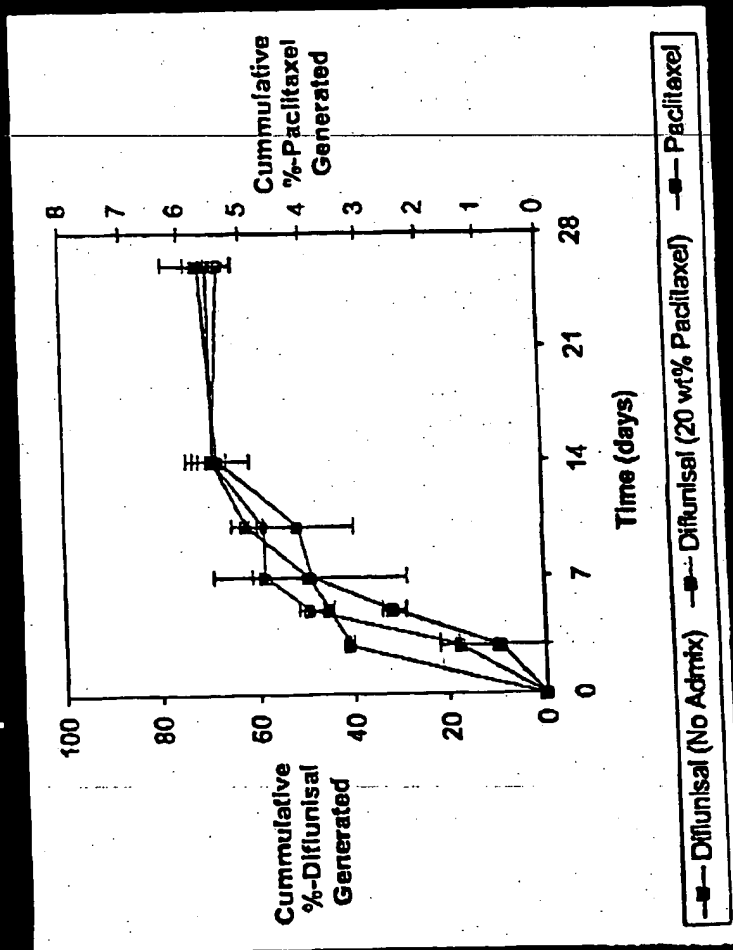
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FIG. 23

# Erosion of PolyAspirin I & II

Diflunisal Generation & Pacitaxel Release into 37 °C Serum from ~5 µm-thick Coatings on 316L SS Plates

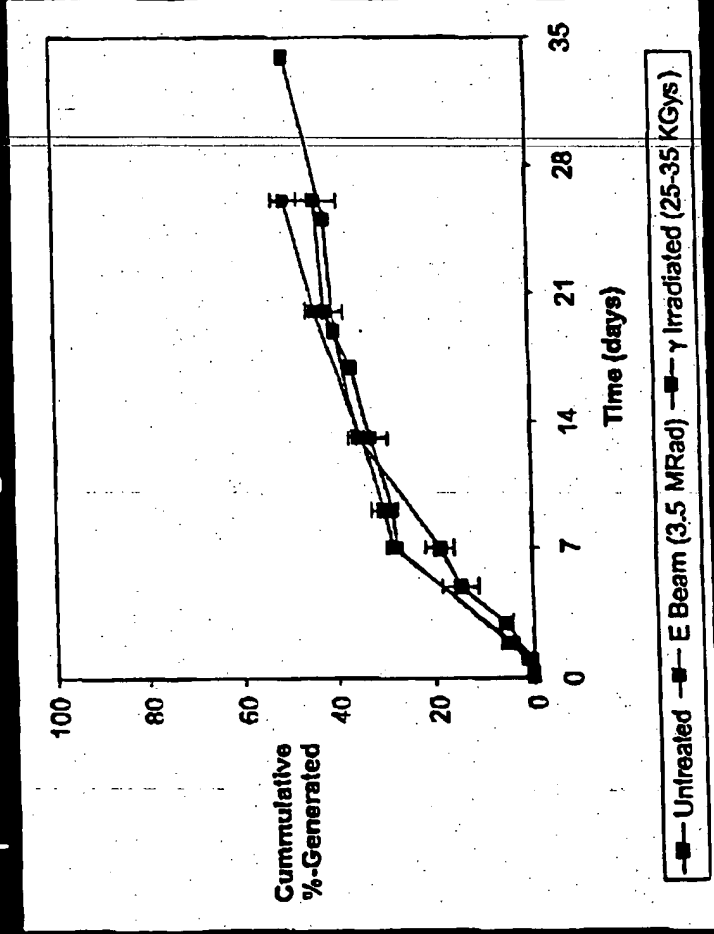


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FIG. 24

# Erosion of Sterilized PolyAspirin II

Generation of Diflunisal into 37 °C Serum from  
~5 µm-thick Coatings on 316L SS Plates



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FIG. 25

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# $\gamma$ Irradiation (25-35 Kgys)

PolyAspirin I

PolyAspirin II

PX261

PX657

$M_w \sim 20K$

$M_w \sim 100K$

Property

MW

N/C

-50%

Hardness

-2 units

-3 units

Flexibility

N/C

.

Adhesion

N/C

.

N/C: no change

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FIG. 26

# E Beam (3-4.5 MRad)

## PolyAspirin I      PolyAspirin II

| Property    | PX657                          |   |
|-------------|--------------------------------|---|
|             | PX261<br>$M_w \sim 20\text{K}$ | $M_w \sim 33\text{K}$ $M_w \sim 80\text{K}$ |
| MW          | -26%                           | +5%      -30%                               |
| Hardness    | -1 unit                        | +2 units      N/C                           |
| Flexibility | N/C                            | -      N/C                                  |
| Adhesion    | -1 unit                        | -      -                                    |

N/C: no change

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FIG. 27

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# Kinetics of NSAID Generation

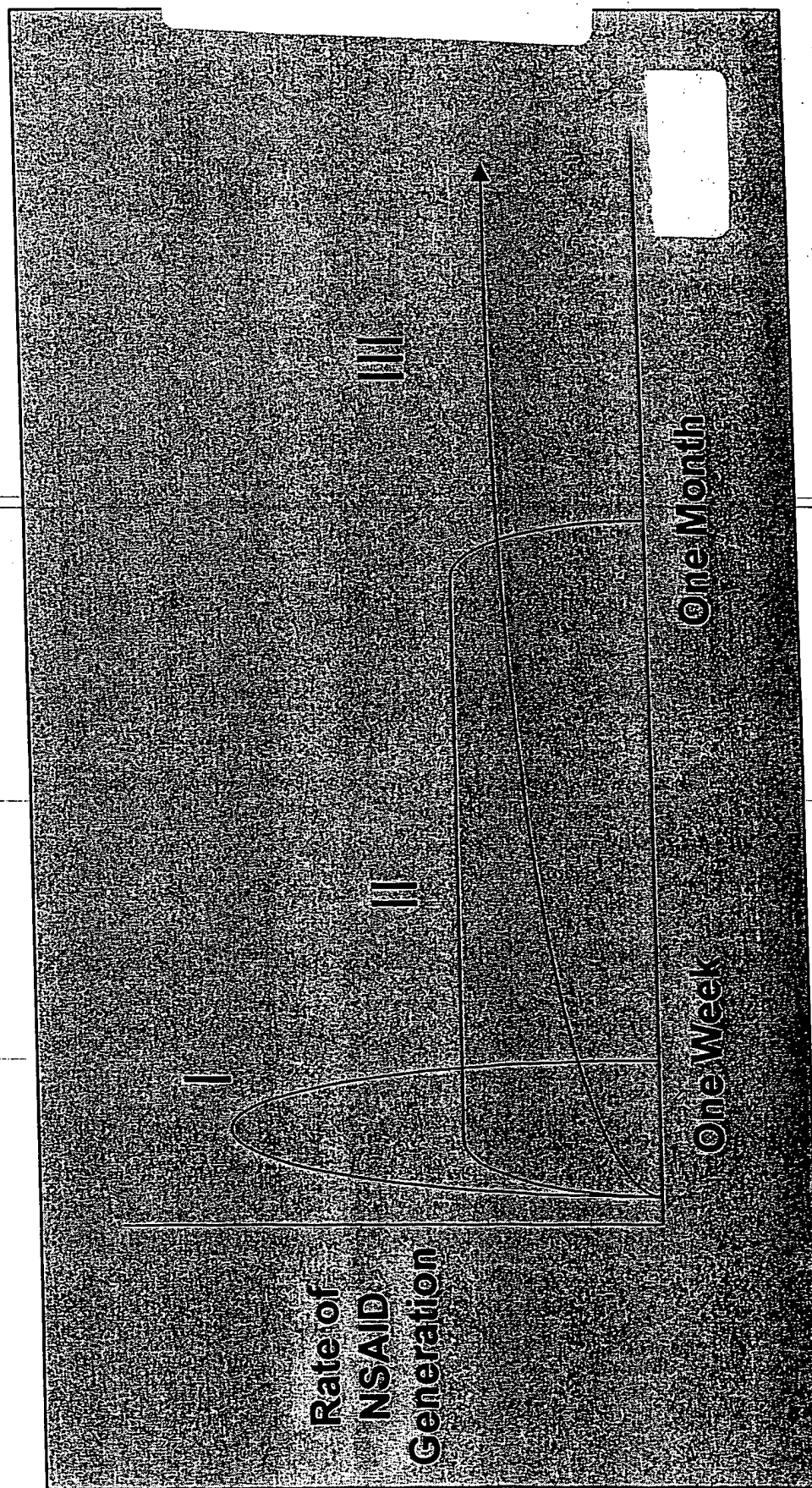
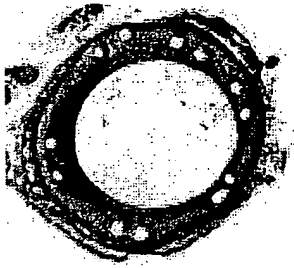
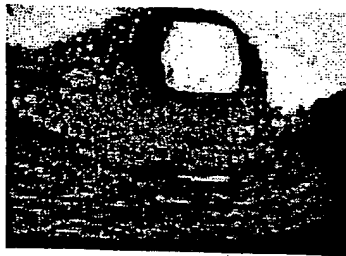
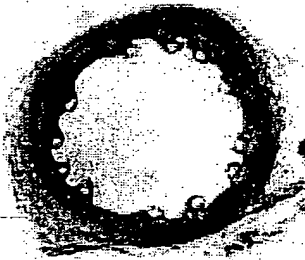


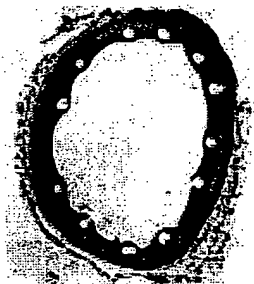
FIG. 28



**FIG. 29**

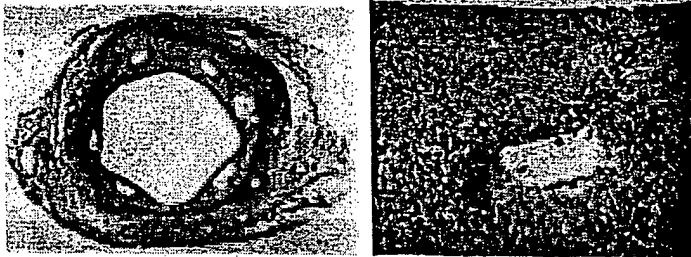


**FIG. 30**



**FIG. 31**

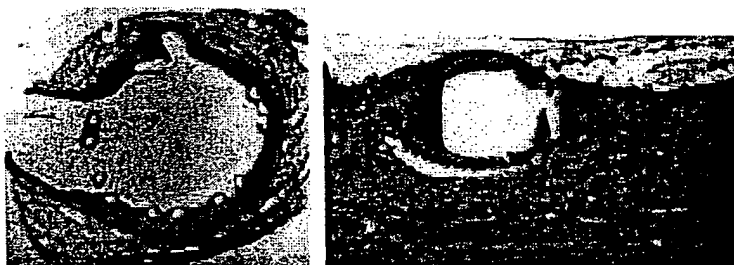




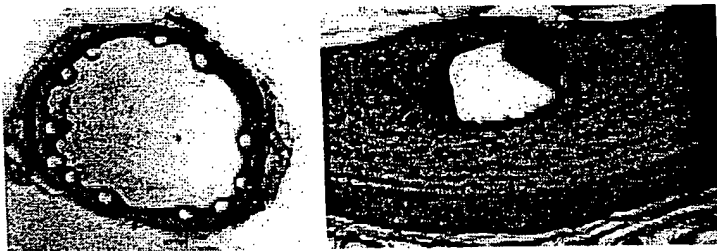
**FIG. 32**



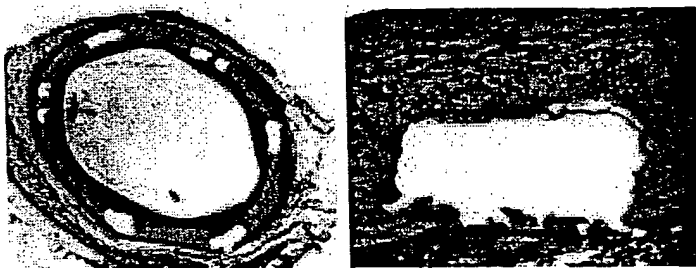
**FIG. 33**



**FIG. 34**



**FIG. 35**

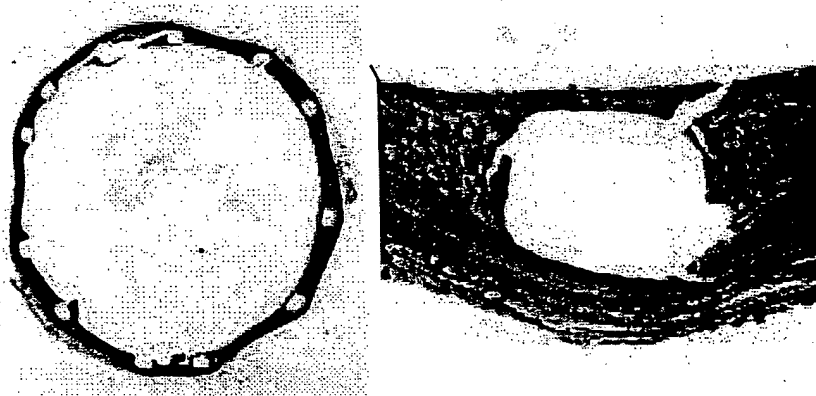


**FIG. 36**

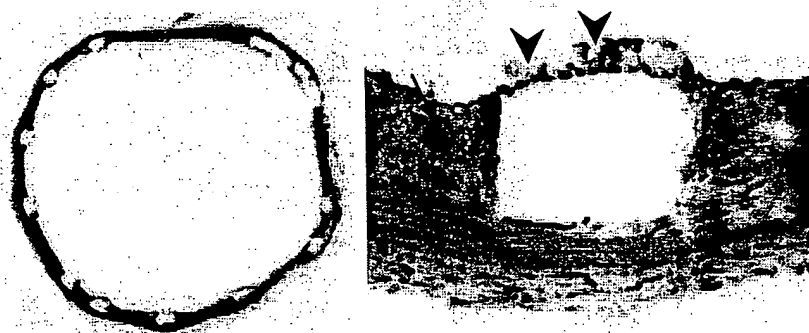
**FIG. 37**

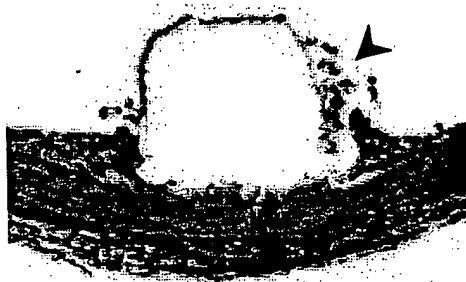
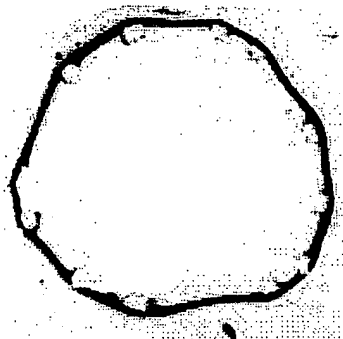


**FIG. 38**

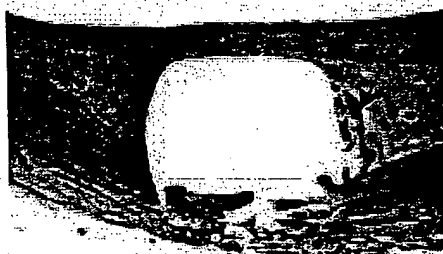
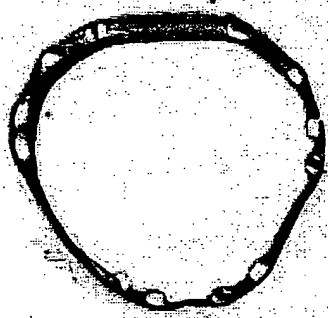


**FIG. 39**

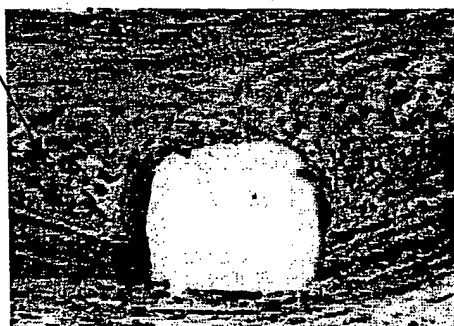
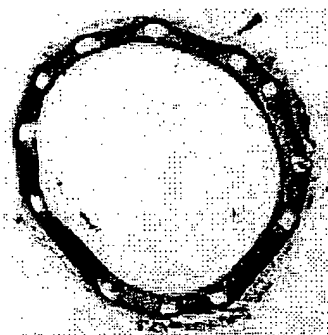




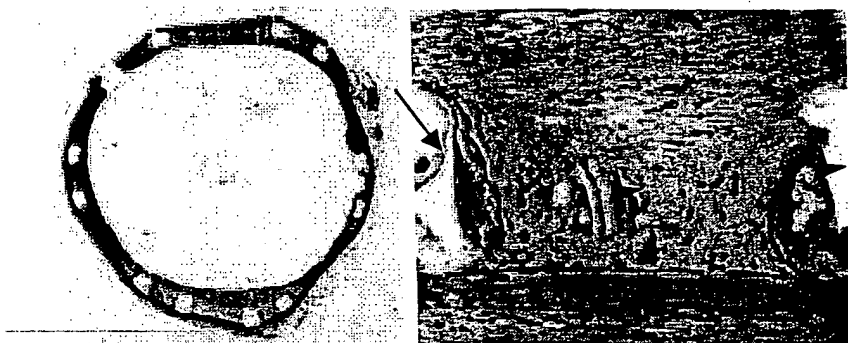
**FIG. 40**



**FIG. 41**



**FIG. 42**



**FIG. 43**

uncrimped/unexpanded

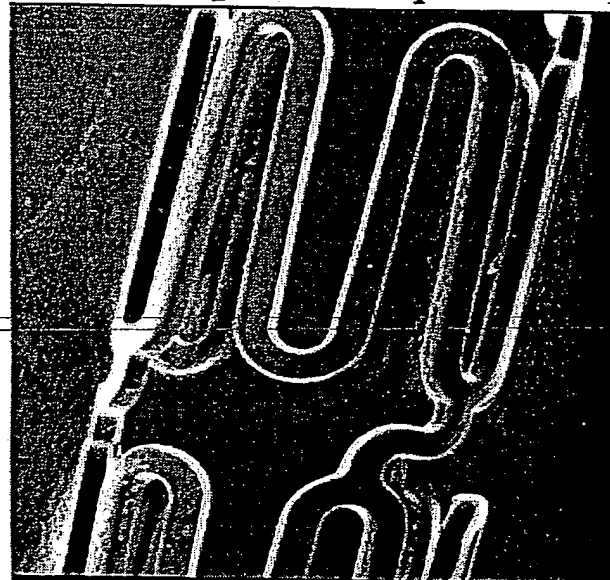


FIG. 44a

15.0 kV 1mm AMRAY

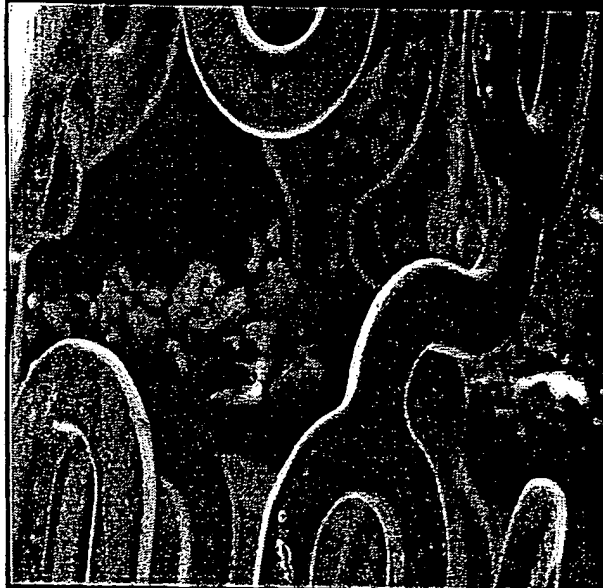
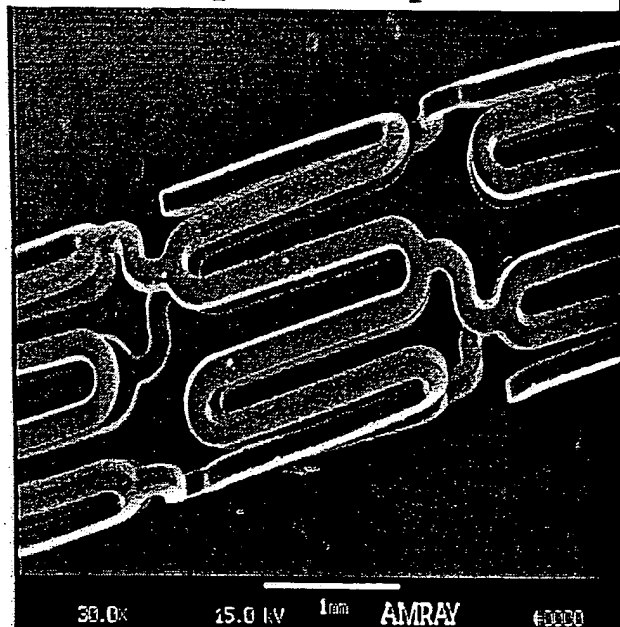


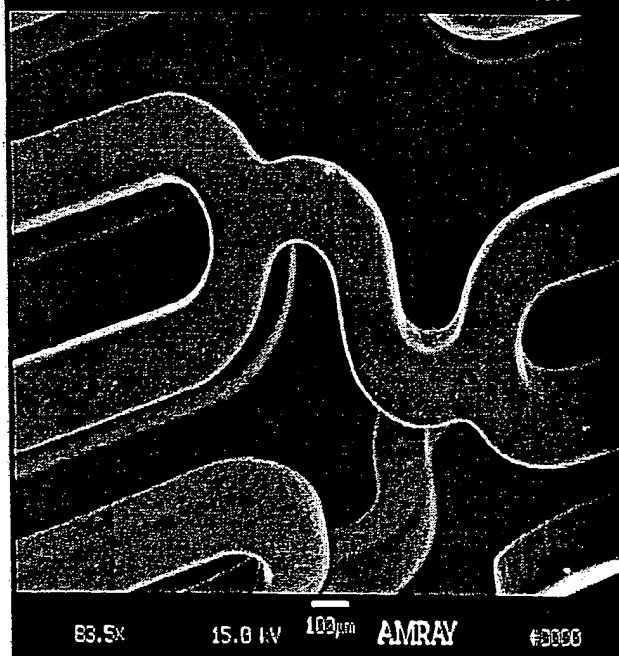
FIG. 44b

85.0x 15.0 kV 102µm AMRAY #3330

uncrimped/unexpanded



**FIG. 45a**



**FIG. 45b**

uncrimped/unexpanded

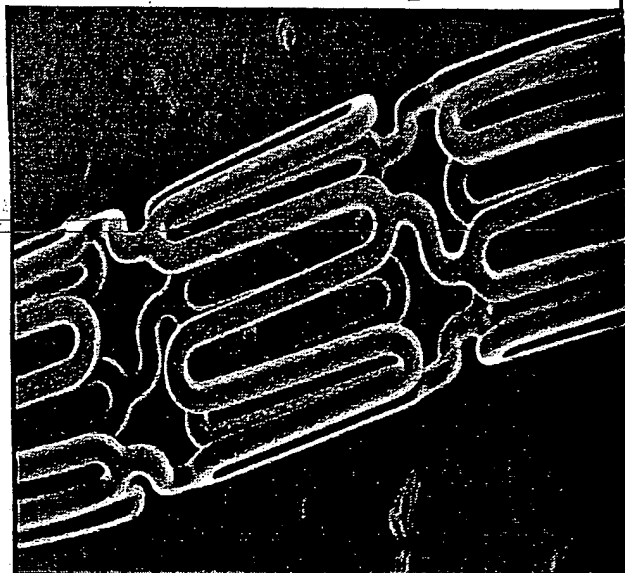


FIG. 46a

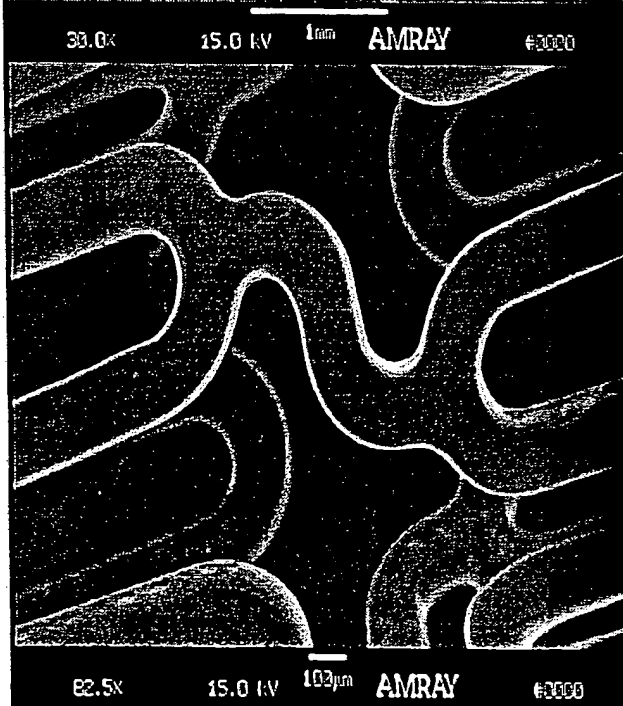


FIG. 46b



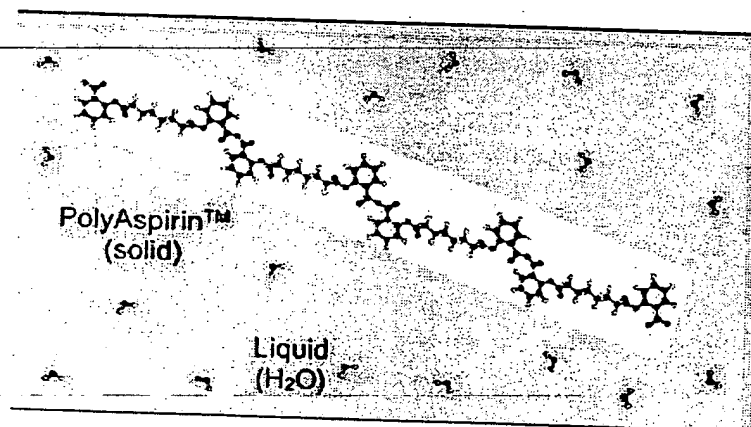


Fig. 47



Fig. 48

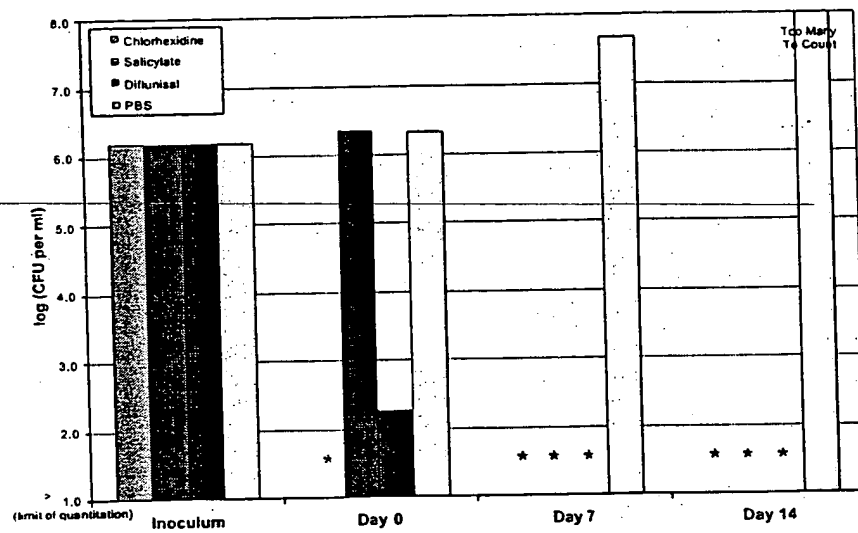


Fig. 49

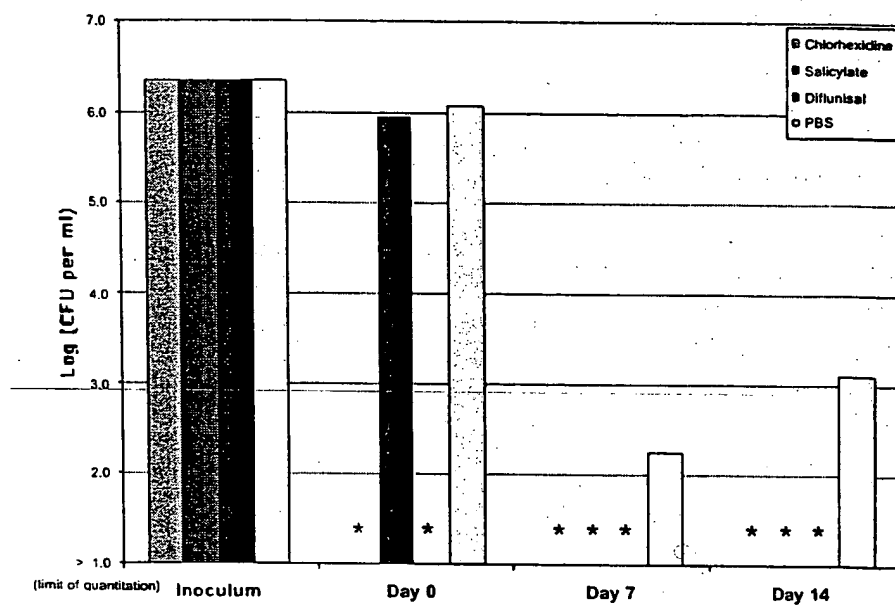


Fig. 50

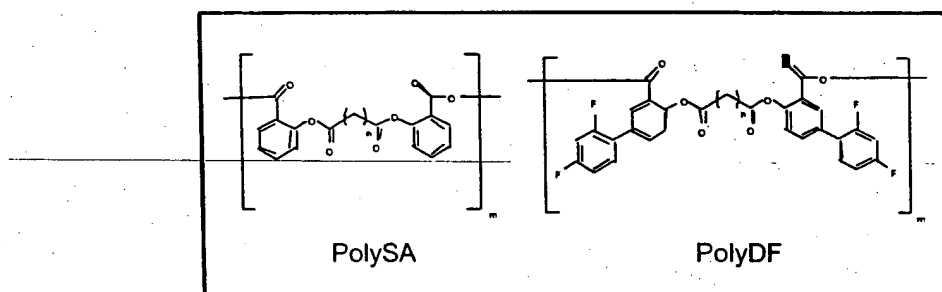


Fig. 51

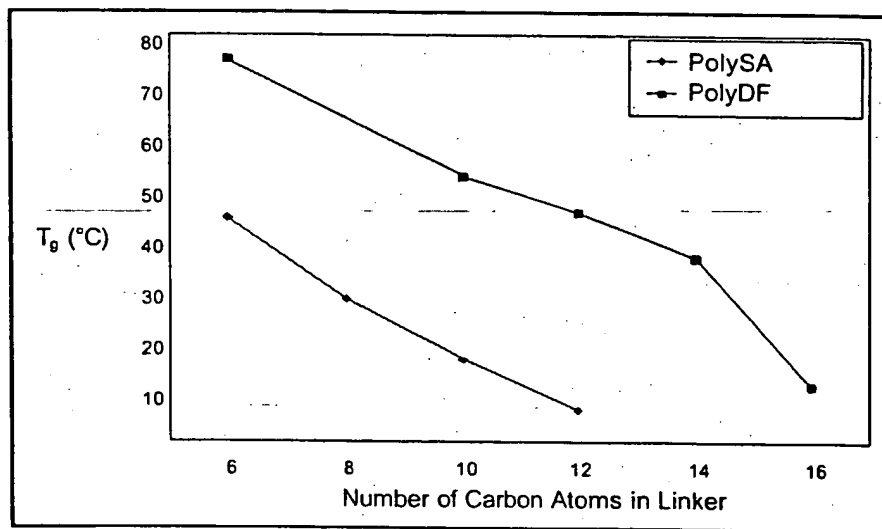


Fig. 52

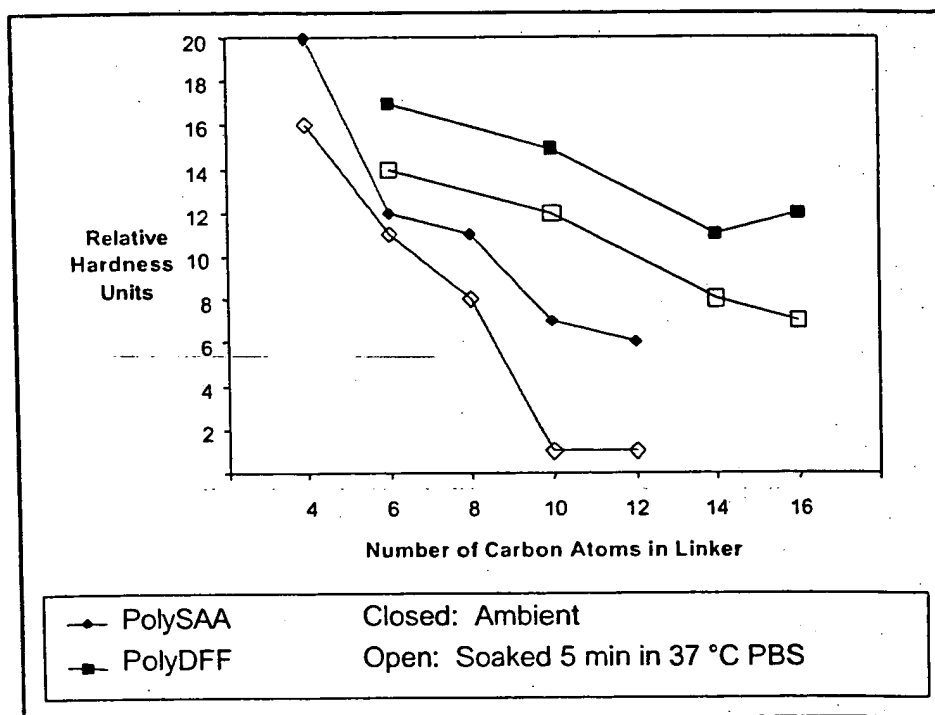


Fig. 53

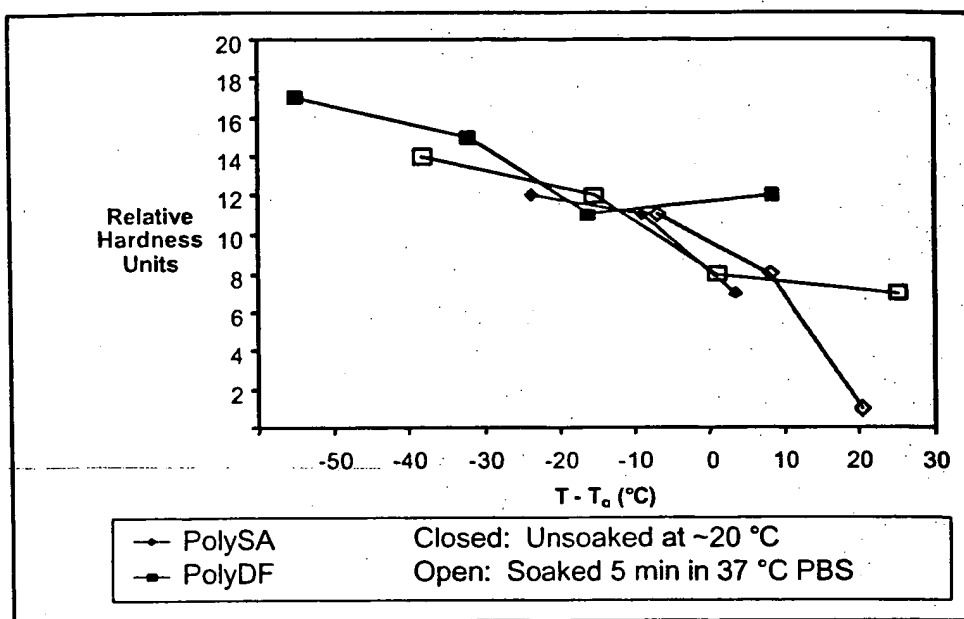


Fig. 54



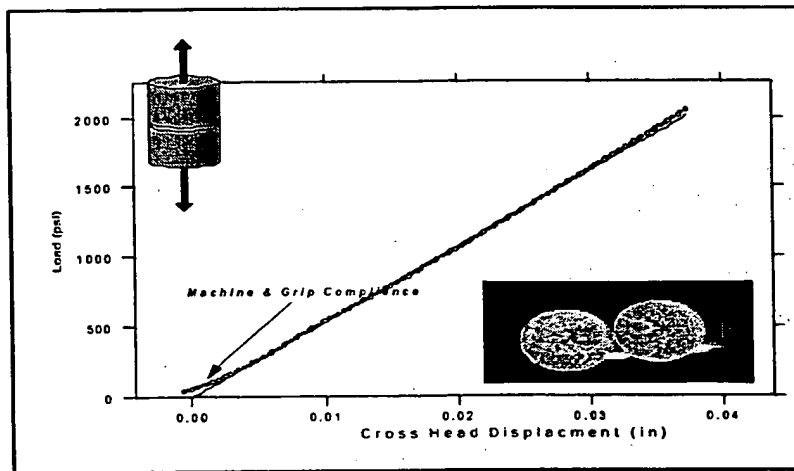


Fig. 55

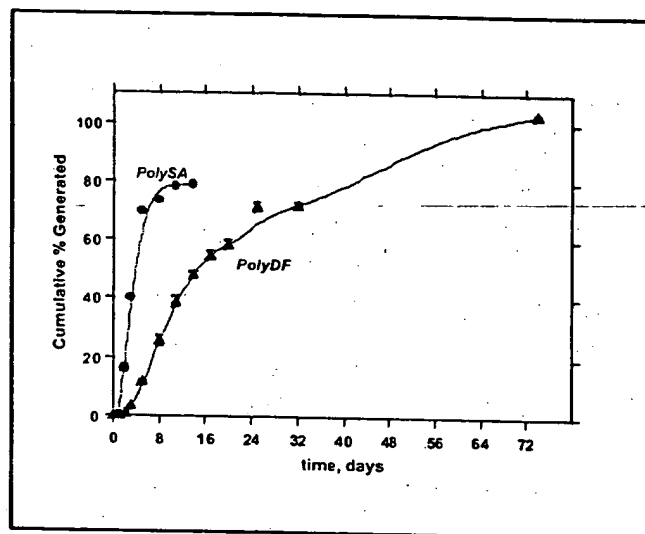


Fig. 56

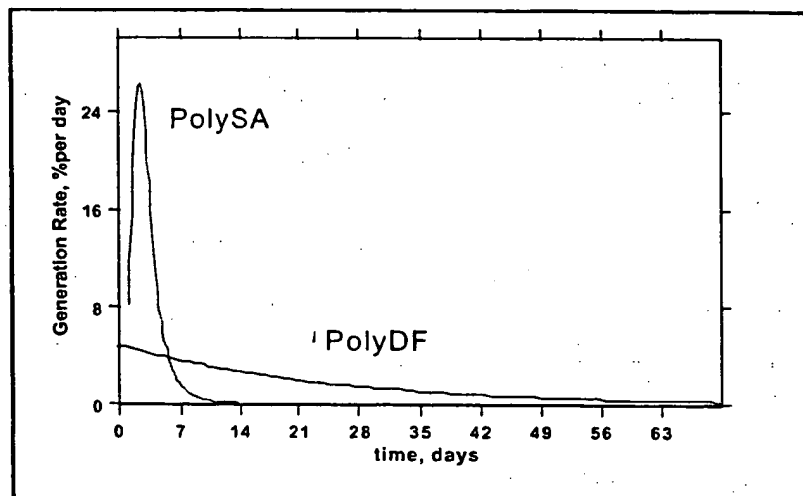


Fig. 57

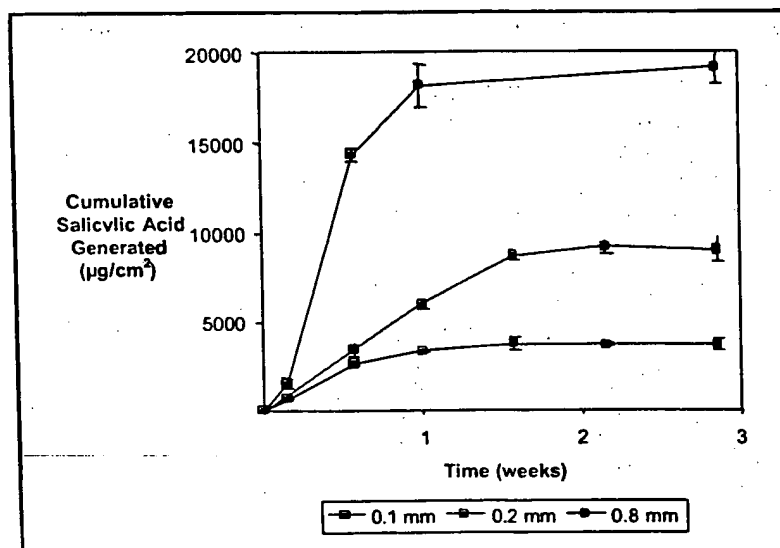


Fig. 58

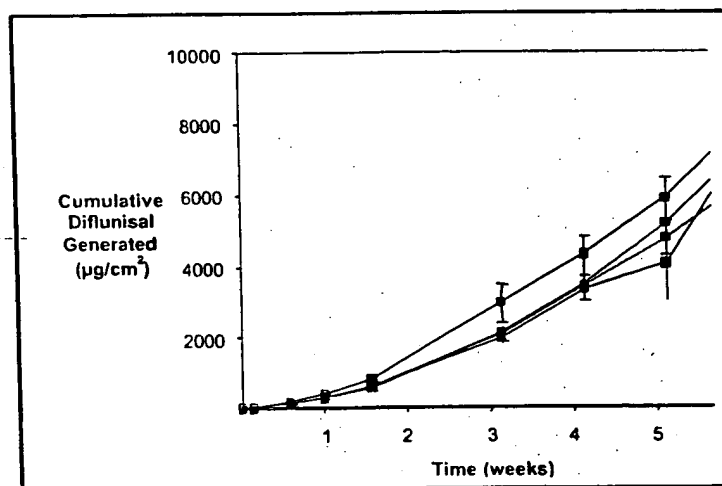


Fig. 59

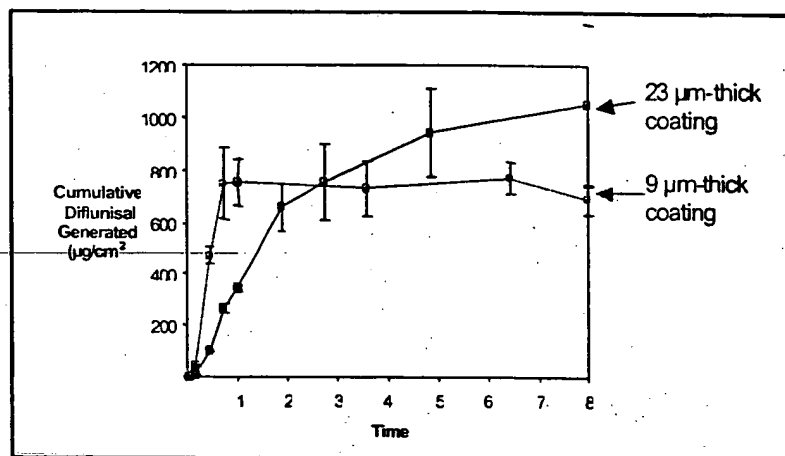


Fig. 60

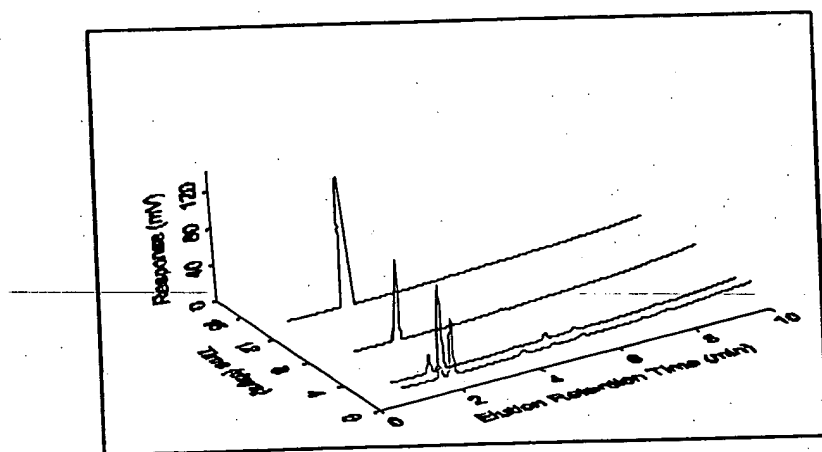


Fig. 61

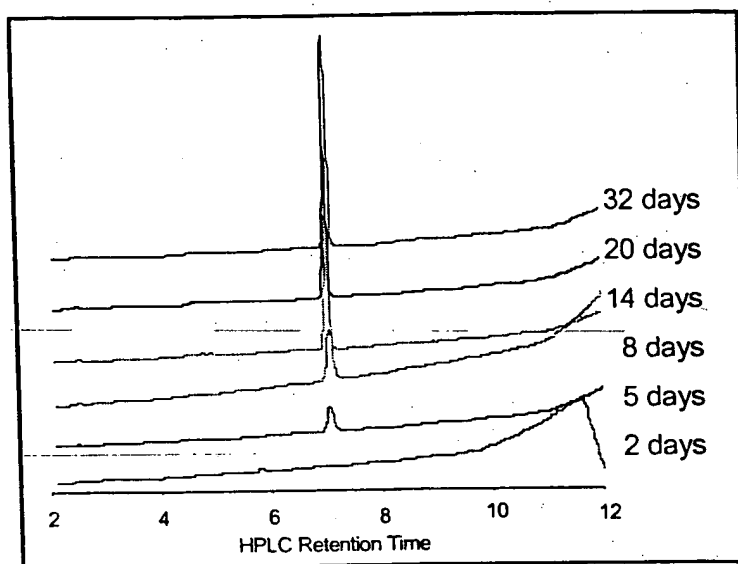


Fig. 62



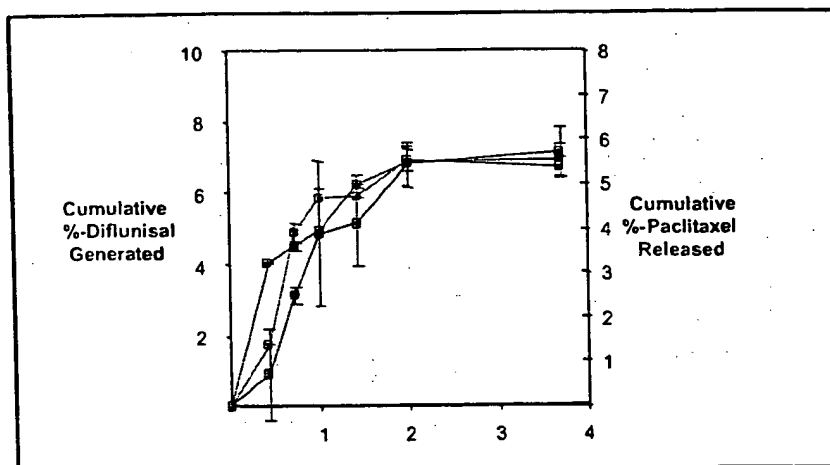


Fig. 63

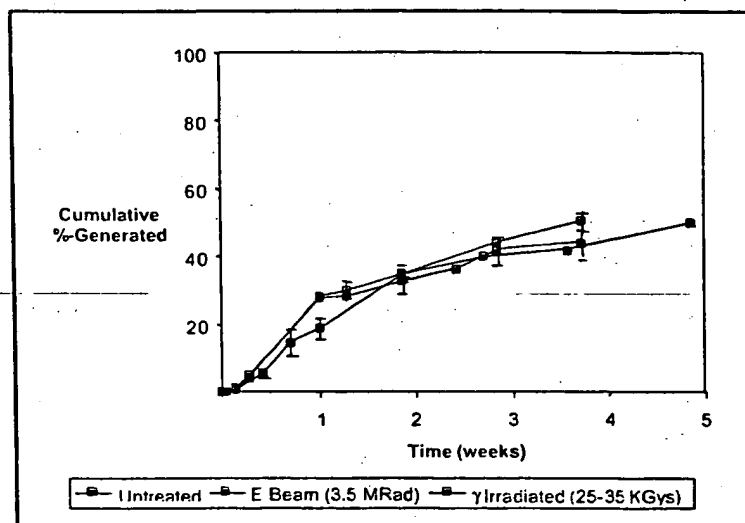


Fig. 64

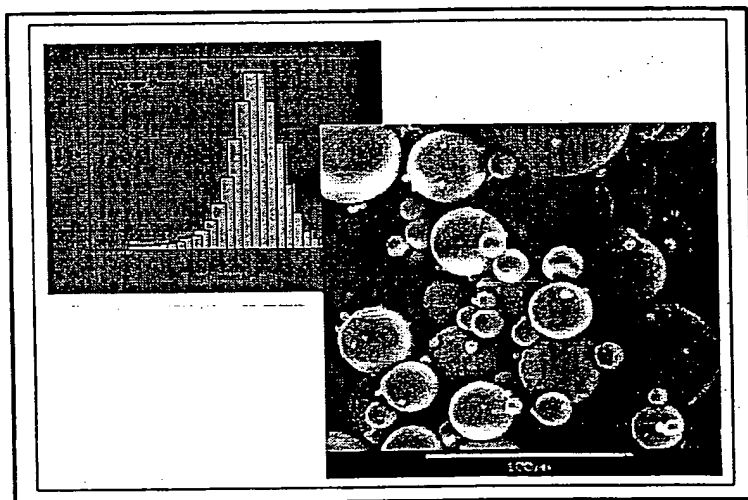


Fig. 65

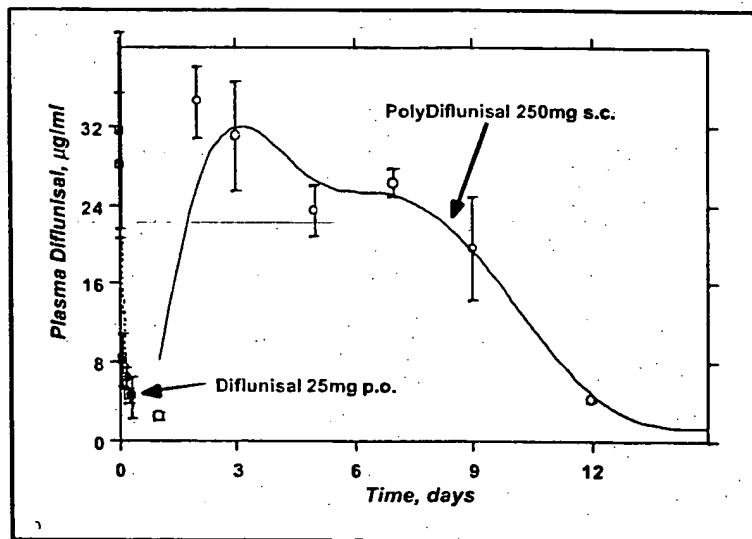


Fig. 66

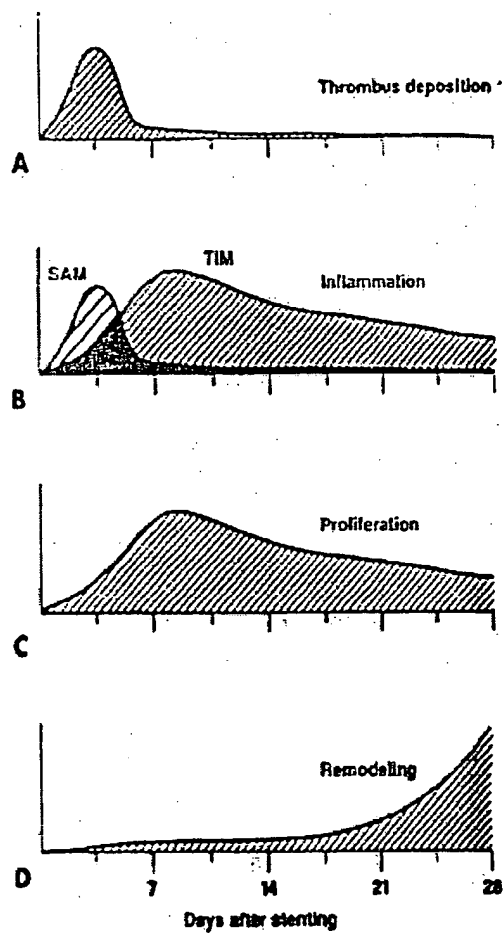


Fig. 67

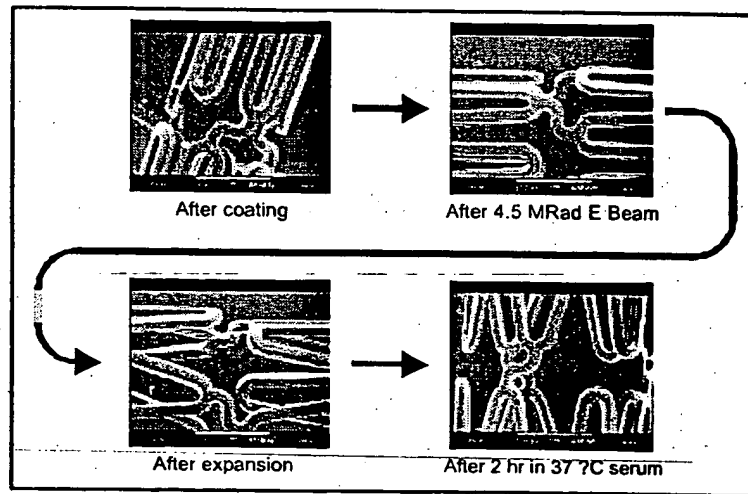


Fig. 68

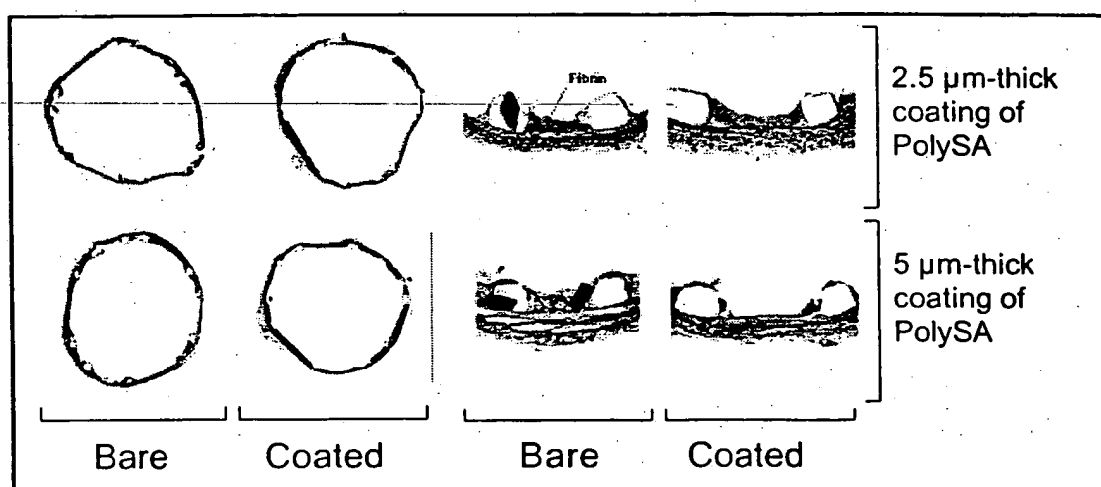


Fig. 69

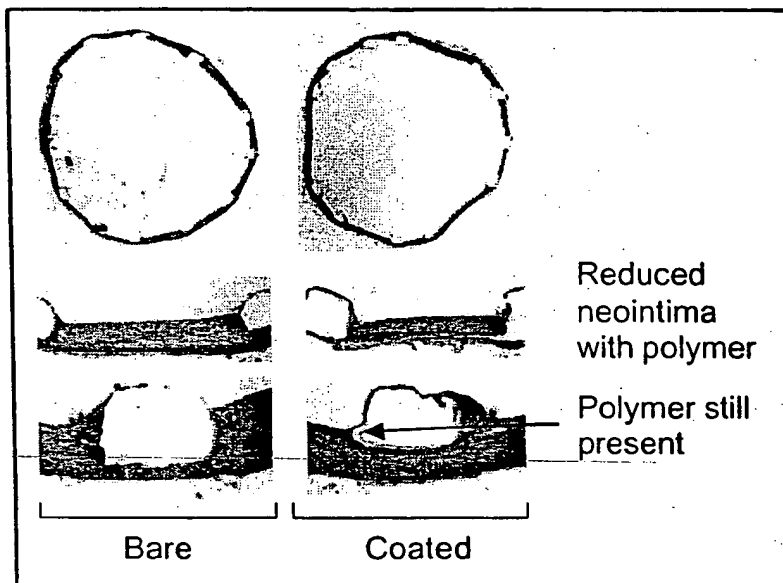


Fig. 70